Page 1

Connecting via Winsock to STN

10/510,435 (Pluse soon) into case)

```
Welcome to STN International! Enter x:x
```

LOGINID:sssptau129pxo

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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* * * * * * * * * * *
                       Welcome to STN International
                   web Page URLs for STN Seminar Schedule - N. America
NEWS
                   "Ask CĂS" for self-help around the clock
NEWS
                   INSPEC enhanced with 1898-1968 archive
          AUG 09
NEWS
      3
          AUG 28
                   ADISCTI Reloaded and Enhanced
NEWS
                   CA(SM)/CAplus(SM) Austrian patent law changes
NEWS
          AUG 30
                   CA/CAplus enhanced with more pre-1907 records CA/CAplus fields enhanced with simultaneous left and right
NEWS
          SEP 11
      6
          SEP 21
NEWS
                   truncation
          SEP 25
                   CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS
                  CAS REGISTRY(SM) no longer includes Concord 3D coordinates
CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
          SEP 25
       9
NEWS
          SEP 25
NEWS 10
                   CEABA-VTB classification code fields reloaded with new
NEWS 11
          SEP 28
                   classification scheme
                   LOGOFF HOLD duration extended to 120 minutes
NEWS 12
          OCT 19
                   E-mail format enhanced
NEWS 13
          OCT 19
                   Option to turn off MARPAT highlighting enhancements available
          OCT 23
NEWS 14
                   CAS Registry Number crossover limit increased to 300,000 in
NEWS 15
          OCT 23
                   multiple databases
                   The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 16
          OCT 23
                   CHEMLIST enhanced with new search and display field
NEWS 17
          OCT 30
          NOV 03
                   JAPIO enhanced with IPC 8 features and functionality
NEWS 18
          NOV 10
                   CA/CAplus F-Term thesaurus enhanced
NEWS 19
                   STN Express with Discover! free maintenance release Version
NEWS 20
          NOV 10
                   8.01c now available
                   CA/CAplus pre-1967 chemical substance index entries enhanced
NEWS 21
          NOV 13
                  with preparation role
                  CAS Registry Number crossover limit increased to 300,000 in
NEWS 22
          NOV 20
                   additional databases
                   CA/CAplus to MARPAT accession number crossover limit increased
          NOV 20
NEWS 23
                   to 50,000
                  CA/CAplus patent kind codes will be updated
          NOV 20
NEWS 24
NEWS EXPRESS
               NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP)
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
               STN Operating Hours Plus Help Desk Availability
NEWS HOURS
               Welcome Banner and News Items
NEWS LOGIN
               For general information regarding STN implementation of IPC 8
NEWS IPC8
NEWS X25
               X.25 communication option no longer available
```

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 02:53:57 ON 27 NOV 2006

=> file reg
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

COST IN U.S. DOLLARS

FILE 'REGISTRY' ENTERED AT 02:54:45 ON 27 NOV 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 24 NOV 2006 HIGHEST RN 913944-64-6 DICTIONARY FILE UPDATES: 24 NOV 2006 HIGHEST RN 913944-64-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10510435.str

L1 STRUCTURE UPLOADED

=> d ll Ll HAS NO ANSWERS Ll STR

Page 3

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 02:58:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE
```

100.0% PROCESSED

0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 0 TO 0 PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> search 11
ENTER TYPE OF SEARCH (SSS), CSS, FAMILY, OR EXACT:.
ENTER SCOPE OF SEARCH (SAMPLE), FULL, RANGE, OR SUBSET:full
FULL SEARCH INITIATED 02:58:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 7 TO ITERATE

100.0% PROCESSED 7 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

Uploading C:\Program Files\Stnexp\Queries\10510435a.str

L4 STRUCTURE UPLOADED

=> d 14

L4 HAS NO ANSWERS L4 STR

Structure attributes must be viewed using STN Express query preparation.

=> s 14

SAMPLE SEARCH INITIATED 03:01:34 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED -0 TO ITERATE

100.0% PROCESSED

0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:

COMPLETE ONLINE

COMPLETE BATCH

PROJECTED ITERATIONS:

0 TO

PROJECTED ANSWERS:

0 TO

L5

0 SEA SSS SAM L4

=> search 14

ENTER TYPE OF SEARCH (SSS), CSS, FAMILY, OR EXACT:.

ENTER SCOPE OF SEARCH (SAMPLE), FULL, RANGE, OR SUBSET: full FULL SEARCH INITIATED 03:01:40 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -7 TO ITERATE

100.0% PROCESSED

7 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

L6,

0 SEA SSS FUL L4

=> s tolteridine

0 TOLTERIDINE

```
Page 5
```

```
=> s tolterodine
L8
                7 TOLTERODINE
=> d 18
      ANSWER 1 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
L8
      209747-05-7 REGISTRY
Entered STN: 11 Aug 1998
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)
RN
ED
OTHER CA INDEX NAMES:
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
      [R-(R*,R*)]-2,3-dihydroxybutanedioate (salt)
OTHER NAMES:
      (R)-Tolterodine L-tartrate
CN
FS
      STEREOSEARCH
MF
      C22 H31 N O . x C4 H6 O6
SR
      STN Files:
                      CA, CAPLUS, CASREACT, IMSPATENTS, IMSRESEARCH, USPATFULL
LC
      CM
            1
           124937-51-5
      CRN
      CMF C22 H31 N O
```

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d 1-7

```
ANSWER 1 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
L8
     209747-05-7 REGISTRY
Entered STN: 11 Aug 1998
RN
ED
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-.
CN
      (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
      [R-(R^*,R^*)]-2,3-dihydroxybutanedioate (salt)
OTHER NAMES:
CN
      (R)-Tolterodine L-tartrate
FS
      STEREOSEARCH
     C22 H31 N O . x C4 H6 O6
MF
SR
     STN Files:
                    CA, CAPLUS, CASREACT, IMSPATENTS, IMSRESEARCH, USPATFULL
LC
     CM
           1
          124937-51-5
     CRN
     CMF C22 H31 N O
Absolute stereochemistry.
                              Rotation (+).
         Ρh
   OH
                    N(Pr-i)_2
  Me
           2
     CM
          87-69-4
     CRN
          С4 Н6 О6
     CMF
Absolute stereochemistry.
       OH
            _C02H
HO2C
          ÖН
                6 REFERENCES IN FILE CA (1907 TO DATE)
                6 REFERENCES IN FILE CAPLUS (1907 TO DATE)
     ANSWER 2 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
L8
     207679-81-0 REGISTRY
Entered STN: 25 Jun 1998
Benzenemethanol, 3-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-hydroxy- (9CI) (CA INDEX NAME)
RN
ED
OTHER NAMES:
     5-Hydroxymethyltolterodine
CN
     PNU 200577
CN
FS
     STEREOSEARCH
```

Page 7

156755-19-0 DR C22 H31 N O2 MF

CI COM SR CA

BIOSIS, CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL STN Files: LC

Absolute stereochemistry. Rotation (+).

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

43 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

43 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ANSWER 3 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN L8

RN

124937-53-7 REGISTRY Entered STN: 26 Jan 1990 ED

Phenol, 2-[(1s)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (S)-

OTHER NAMES:

(S)-Tolterodine CN STEREOSEARCH FS

C22 H31 N O MF

CICOM

SR CA

STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT7, USPATFULL

Absolute stereochemistry. Rotation (-).

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
L8
      ANSWER 4 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN
RN
      124937-52-6 REGISTRY
      Entered STN: 26 Jan 1990
ED
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
       (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
      Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (R)-, [R-(R*,R*)]-2,3-dihydroxybutanedioate (1:1) (salt)
       (R)-Tolterodine L-tartrate
CN
      Detrol
CN
      Detrusitol
CN
      PNU 200583E
CN
CN
      Tolterodine tartrate
CN
      Tolterodinium (+)-(2R,3R)-hydrogen tartrate (1:1)
FS
      STEREOSEARCH
      C22 H31 N O . C4 H6 O6
MF
CI
      COM
SR
      CA
        TN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, IMSCOSEARCH, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PATDPASPC, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPATZ, USPATFULL
LC
      STN Files:
            (*File.contains numerically searchable property data)
      CM
             1
      CRN
            124937-51-5
      CMF C22 H31 N O
```

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
              82 REFERENCES IN FILE CA (1907 TO DATE)
              82 REFERENCES IN FILE CAPLUS (1907 TO DATE)
     ANSWER 5 OF 7 REGISTRY COPYRIGHT 2006 ACS ON STN
L8
     124937-51-5 REGISTRY
Entered STN: 26 Jan 1990
RN
ED
     Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-
            (CA INDEX NAME)
OTHER CA INDEX NAMES:
     Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (R)-
CN
OTHER NAMES:
     (+)-Tolterodine
CN
CN
     (R)-(+)-Tolterodine
     (R)-N,N-Diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropanamine
CN
     (R)-N,N-Diisopropyl-N-[3-(2-hydroxy-5-methylphenyl)-3-phenylpropyl]amine
CN
     (R)-Tolterodine
CN
CN
     Kabi 2234
     PNU 200583
CN
CN
     Tolterodine
     STEREOSEARCH
FS
     215929-30-9
DR
     C22 H31 N O
MF
CI
     COM
SR
     CA
LC
     STN Files:
                  ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,
       CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE,
       IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT,
       PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:
                      WHO
```

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

267 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
268 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L8 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN RN 124936-75-0 REGISTRY ED Entered STN: 26 Jan 1990 CN Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,

Page 10

hydrochloride (9CI) (CA INDEX NAME) OTHER NAMES: (+-)-Tolterodine hydrochloride CN N,N-Diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropylamine CN hvdrochloride C22 H31 N O . C] H MF SR CA ADISINSIGHT, CA, CAPLUS, CASREACT, IMSPATENTS, IMSRESEARCH, LC STN Files: TOXCENTER, USPATFULL CRN (124936-74-9)

● HC1

5 REFERENCES IN FILE CA (1907 TO DATE) 5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

ANSWER 7 OF 7 REGISTRY COPYRIGHT 2006 ACS on STN **L8** 124936-74-9 REGISTRY Entered STN: 26 Jan 1990 RN ED Phenol, 2-[3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl- (9CI) CN (CA INDEX NAME) OTHER NAMES: N,N-Diisopropyl-N-[3-(2-hydroxy-5-methylphenyl)-3-phenylpropyl]amine CN Racemic tolterodine CN MF C22 H31 N O CI COM SR CA LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, PS, TOXCENTER, USPAT2, **USPATFULL**

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

20 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

20 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
=> s 124937-52-6
                 1 124937-52-6
L9
                      (124937-52-6/RN)
=> s 209747-05-7
                 1 209747-05-7
L10
                      (209747-05-7/RN)
=> file caplus
                                                                SINCE FILE
COST IN U.S. DOLLARS
                                                                                      TOTAL
                                                                       ENTRY
                                                                                   SESSION
                                                                      369.60
                                                                                    369.81
FULL ESTIMATED COST
FILE 'CAPLUS' ENTERED AT 03:10:42 ON 27 NOV 2006
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Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:
http://www.cas.org/infopolicy.html
=> 5 19
L11
               82 L9
=> s 110
                 6 L10
L12
=> s 112 not 111
                 6 L12 NOT L11
L13
=> d 111 1-82 fbib ab hitstr
      ANSWER 1 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2006:1073192 CAPLUS
DN
      145:425975
      Method for manufacturing tolterodine tartrate soft capsule
TI
      Wan, Liuyi
IN
PA
      Peop. Rep. China
      Faming Zhuanli Shenqing Gongkai Shuomingshu, 6pp.
SO
      CODEN: CNXXEV
DT
      Patent
ΙA
      Chinese
FAN.CNT 1
```

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE						
PI	CN 1709231	Α	20051221	CN 2005-10080363 CN 2005-10080363	20050704 20050704						
AB	The title tolterodine tartrate soft capsule comprises a solution or suspension content which includes tolterodine tartrate and at least one substance selected from the group including solvent (preferably PEG400 or soybean oil), solution adjuvant (preferably propylene glycol), suspending agent (PEG6000), solubilizer (preferably NaOH solution or oleic acid), and surfactant (Span-80, Tween-80, etc).										
IT	124937-52-6, Tolterodine tartrate RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method for manufacturing tolterodine tartrate soft capsule)										
RN CN	124937-52-6 CAPLUS Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)										
	· CM 1										
	CRN 124937-51-5 CMF C22 H31 N O										

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
L11 ANSWER 2 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:1006721 CAPLUS
DN 145:383488
TI Methods and compositions containing bicifadine for the treatment of urinary incontinence
IN Skolnick, Phil
PA Dov Pharmaceutical, Inc., USA
SO PCT Int. Appl., 50pp.
```

```
CODEN: PIXXD2
DT
       Patent
       English
LA
FAN.CNT 1
                                     KIND
       PATENT NO.
                                               DATE
                                                                 APPLICATION NO.
                                                                                                    DATE
                                                20060928
                                                                 wo 2006-us9638
                                                                                                    20060317
ΡI
       wo 2006102029
                                      A2
       WO 2006102029
                                      Α3
                                                20061109
                  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
                   MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
                   SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
                   VN, YU, ZA, ZM, ZW
             RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
                   IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
                   CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                   KG, KZ, MD, RU, TJ, TM
                                                                  US 2005-664002P
       Methods and compns. containing bicifadine are provided for the prevention and
AB
       treatment of lower urinary tract disorders in mammalian subjects. The methods and compns. may be used to prevent or treat urinary incontinence, urinary urgency, nocturia, and enuresis associated with neurogenic and non-neurogenic overactive bladder, interstitial cystitis, prostatitis, and
       benign prostatic hyperplasia, among other conditions. Addnl. compns. and
       methods are provided which employ bicifadine in combination with a second
       anti-incontinence agent, or a different therapeutic agent to yield more
       effective anti-incontinence treatment tools, and/or dual activity therapeutic methods and formulations useful to prevent or reduce urinary
       incontinence and one or more addnl. symptoms such as urinary urgency, overflow, frequency, or pain in mammalian subjects. Bicifadine-HC l was prepared in a series of steps starting from p-tolylacetic acid. This was converted to polymorph form B by using isopropanol.
IT
       124937-52-6. Tolterodine tartrate
       RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
        (Biological study); USES (Uses)
            (methods and compns. containing bicifadine for treatment of urinary
            incontinence)
RN
       124937-52-6 CAPLUS
       Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
       (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
       CM
              1
              124937-51-5
       CRN
              C22 H31 N O
       CMF
```

```
CM 2
```

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
ANSWER 3 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN
       2006:918812 CAPLUS
ΑN
        145:299643
DN
       Antibiotic and combinations of antibiotic and symptomatic relief agent
TI
        formulations
       Evans, Donald L.; Bryant, Thomas J.; Ping, Jeffrey H.; Roberts, Richard Howard; Sirico, William J.; Arnold, Kristin; Davis, Matthew William; Hayer, Gregory Keith; Nielsen, Kurt R. Mutual Pharmaceutical Company, Inc., USA
IN
PA
        PCT Int. Appl., 72pp.
SO
       CODEN: PIXXD2
DT
        Patent
       English
LA
FAN.CNT 1
       PATENT NO.
                                      KIND
                                                 DATE
                                                                  APPLICATION NO.
                                                                                                      DATE
PΙ
       wo 2006093784
                                       Α2
                                                 20060908
                                                                  wo 2006-US6412
                                                                                                      20060224
                   AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
                   KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
                   MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
                   SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
                   VN, YU, ZA, ZM, ZW
             RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
                   IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
                                                                   US 2005-656496P
                                                                                                      20050225
                                                                   US 2005-671979P
                                                                                                      20050415
                                                                                                  Р
                                                                   US 2006-362547
       us 2006205682
                                       Α1
                                                 20060914
                                                                                                      20060224
                                                                   US 2005-656496P
                                                                                                      20050225
                                                                   us 2005-671979P
                                                                                                 P 20050415
       Disclosed herein are antibiotic formulations and combinations of
AB
       antibiotic and symptomatic relief agent formulations. The combinations
       are suitable to treat a variety of diseases, including an infection, while treating the symptoms associated with the disease. Also disclosed are methods of treating a disease or an infertion and its symptoms, as well as pharmaceutical kits containing such formulations. Tablets contained
       trimethoprim 80, and sulfamethoxazole 400 mg.
IT
       124937-52-6, Tolterodine tartrate
```

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibiotic and combinations of antibiotic and symptomatic relief agent

formulations)
RN 124937-52-6 CAPLUS
CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5
CMF C22 H31 N 0

Absolute stereochemistry. Rotation (+).

CRN 87-69-4 CMF C4 H6 06

Absolute stereochemistry.

ANSWER 4 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN 2006:742863 CAPLUS AN 145:152914 DN Stability-indicating HPLC determination of tolterodine tartrate in TI pharmaceutical dosage form Saxena, Vinay; Zaheer, Zahid; Farooqui, Mazhar ΑU Maulana Azad College, Aurangabad, 431 001, India Indian Journal of Chemical Technology (2006), 13(3), 242-246 CS S0 CODEN: ICHTEU; ISSN: 0971-457X
National Institute of Science Communication and Information Resources РΒ DT Journal English LA A simple, selective, precise and stability-indicating high-performance AB liquid chromatog. (HPLC) method of anal. tolterodine tartrate in pharmaceutical dosage form was developed and validated. The chromatog. conditions comprised a reversed-phase C18 column (250 + 4.6 mm), 5 μ with a mobile phase consisting of a mixture of buffer solution (2.88 g ammonium dihydrogen orthophosphate in 1 L of water) and methanol in the ratio of 40: 60. Triethylamine (5 mL/L) was added to it and pH of mobile phase was adjusted to 7.0 \pm 0.1 with orthophosphoric acid at a flow rate of 1.5 mL/min. Detection was carried out at 220 nm. The retention

time of tolterodine was 6.49 min. The linear regression anal. data for the calibration plots showed good linear relationship with coefficient of regression value, r2 = 0.99 in the concentration range 200.60-601.80 µg per mL. The value of correlation coefficient, slope and intercept were 1.0, 20.87 and -6.87, resp. The method was validated for precision, recovery, ruggedness and robustness. The drug undergoes degradation under acidic, basic, photochem. and thermal conditions. All the peaks of degraded product were resolved from the active pharmaceutical ingredient with significantly different retention time. The samples degraded with hydrogen peroxide showed no addnl. peak. This indicates that the drug is susceptible to acid-base hydrolysis, photochem. and thermal degradation statistical anal. proves that the method is reproducible and selective for the estimation of said drug. As the method could effectively sep. the drug from its degradation product, it can be employed as a stability-indicating

IT 124937-52-6, Tolterodine tartrate

RL: ANT (Analyte); ANST (Analytical study)
(stability-indicating HPLC determination of tolterodine tartrate in pharmaceutical dosage form)

RN 124937-52-6 CAPLUS CN Phenol, 2-[(1R)-3-[b

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

```
2006:687413 CAPLUS
AN
      145:195647
DN
      Tolterodine tartrate dripping pill and its preparation method
TI
      Zhang, Xiaoming; Wang, Jun; Wu, Yuanyan
Zhuhai Skypharm Technology Development Co., Ltd., Peop. Rep. China
IN
PA
      Faming Zhuanli Shenging Gongkai Shuomingshu, 6 pp.
S<sub>0</sub>
      CODEN: CNXXEV
      Patent
DT
      Chinese
LΑ
FAN.CNT 1
      PATENT NO.
                                KIND
                                         DATE
                                                        APPLICATION NO.
                                                                                     DATE
                                ____
      CN 1686095
                                         20051026
                                                        CN 2005-10034026
                                                                                     20050412
PΙ
                                 Α
                                                        CN 2005-10034026
                                                                                     20050412
      The invention relates to a tolterodine tartrate dripping pill, which
AΒ
      comprises 0.5-25% of tolterodine tartrate and 75-99.5% of matrix. The
      preparation method comprises adding tolterodine tartrate to melted matrix, mixing to even, dripping into a cooling to obtain dripping pills, and drying. The inventive dripping pill can disintegrate rapidly and is especially
      suitable for children, the elderly, bed patients, and patients with
      dysphagia.
IT
      124937-52-6, Tolterodine tartrate
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (tolterodine tartrate dripping pill and its preparation)
      124937-52-6 CAPLUS
RN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R, 3R) -2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
            124937-51-5
      CRN
           C22 H31 N O
      CMF
```

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
ANSWER 6 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2006:687412 CAPLUS
ΑN
      145:174294
DN
      Sustained-release tolterodine tartrate dripping pill and its preparation
TI
      Zhang, Xiaoming; Wang, Jun; Ding, Feng; Wu, Yuanyan
Zhuhai Skypharm Technology Development Co., Ltd., Peop. Rep. China
IN
PA
      Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
SO
      CODEN: CNXXEV
DT
      Patent
      Chinese
LA
FAN.CNT 1
                                                         APPLICATION NO.
                                                                                        DATE
      PATENT NO.
                                KIND
                                          DATE .
                                                         CN 2005-10034025
PΙ
      CN 1686094
                                  Α
                                          20051026
                                                                                        20050412
                                                         CN 2005-10034025
                                                                                        20050412
      The invention relates to a sustained-release tolterodine tartrate dripping
AB
      pill which comprises tolterodine tartrate 2-20%, hydrophobic matrix 1-30%,
      and hydrophilic matrix 40-98%. The preparation method comprises heating and melting the matrixes, adding tolterodine tartrate to form a suspension, dripping into a cooling agent to obtain dripping pills, and drying.

124937-52-6, Tolterodine tartrate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
IT
          (Sustained-release tolterodine tartrate dripping pill and its preparation
          method)
      124937-52-6 CAPLUS
RN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R.3R)-2.3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
      CRN
            124937-51-5
      CMF C22 H31 N O
```

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

OH -

```
_CO2H
           OH
     ANSWER 7 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2006:677667
AN
                    CAPLUS
      145:130840
DN
      Process for preparing tolterodine tartrate
TI
      Kovacs, Laszlo Zsolt; Szabo, Csaba; Molnarne, Erika Magyar; Singer, Claude
ΙN
      Teva Pharmaceutical Industries, Ltd., Israel; Teva Pharmaceuticals Usa,
PA
SO
      PCT Int. Appl., 19 pp.
      CODEN: PIXXD2
DT
      Patent
      English
LA
FAN.CNT 2
      PATENT NO.
                             KIND
                                      DATE
                                                    APPLICATION NO.
                                                                                DATE
     wo 2006074479
                                      20060713
                                                    wo 2006-US917
                                                                                20060110
PΙ
                              Α1
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
               CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
               GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
               KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
               MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
               SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
               VN, YU, ZA, ZM, ZW
          RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
                                                    US 2005-642866P
                                                                                20050110
                                                    US 2005-690823P
                                                                                20050614
     US 2006194876
                               Α1
                                      20060831
                                                    us 2006-329915
                                                                                20060110
                                                    US 2005-642866P
                                                                                20050110
                                                    US 2005-690823P
                                                                                20050614
                                                    US 2006-329922
                                                                                20060110
     US 2006194987
                               Α1
                                      20060831
                                                    US 2005-642866P
                                                                                20050110
                                                                            P
                                                    US 2005-690823P
                                                                                20050614
PATENT FAMILY INFORMATION:
FAN 2006:677666
      PATENT NO.
                             KIND
                                      DATE
                                                    APPLICATION NO.
                                                                                DATE
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ΡI	WO	2006074478 A1			20060713			wo 2006-US916					20060110					
		W:	ΑE,	AG,	AL,	ΑM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,
			CN,	co,	CR,	cu,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
			GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KM,	KΝ,	KΡ,	KR,
			ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	LY,	MA,	MD,	MG,	MK,	MN,	MW,	ΜX,
			ΜZ,	NA,	NG,	ΝI,	NO,	ΝZ,	OM,	PG,	РΗ,	PL,	PΤ,	RO,	RU,	sc,	SD,	SE,
			SG,	SK,	SL,	SM,	SY,	TJ,	TM,	TN,	TR,	TT,	ΤZ,	UA,	UG,	US,	UΖ,	VC,
				•	,	ZM,												
		RW:	AT,	ΒE,	ΒG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	FI,	FR,	GB,	GR,	HU,	ΙE,
																	BF,	
		•	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG,	BW,	GH,
			GM,	ΚE,	LS,	MW,	ΜZ,	NΑ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
			KG,	ΚZ,	MD,	RU,	TJ,	TM										

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20050110
                                                   US 2005-642866P
                                                   US 2005-690823P
                                                                              20050614
      us 2006194876
                              Α1
                                     20060831
                                                   us 2006-329915
                                                                              20060110
                                                   US 2005-642866P
                                                                              20050110
                                                   US 2005-690823P
                                                                              20050614
                                                                              20060110
      US 2006194987
                                     20060831
                                                   us 2006-329922
                              Α1
                                                   US 2005-642866P
                                                                              20050110
                                                   US 2005-690823P
                                                                              20050614
      The invention encompasses processes for making tolterodine tartrate.
AB
     Tolterodine hydrobromide was prepared and treated with KOH to give the free base. L-Tartaric acid was dissolved in EtOH and treated with the
      tolterodine to give the title compound
      124937-52-6P
IT
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
         (process for preparing tolterodine tartrate)
RN
      124937-52-6 CAPLUS
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
      CRN
           124937-51-5
      CMF
           C22 H31 N O
```

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:677666 CAPLUS

DN 145:130977

TI Substantially pure tolterodine tartrate and process for preparing thereof

```
Kovacs, Laszlo Zsolt; Szabo, Csaba; Molnarne, Erika Magyar; Singer, Claude
IN
      Teva Gyogyszergyar Reszvenytarsasag, Hung.; Teva Pharmaceuticals Usa,
PA
      Inc.; Teva Pharmaceutical Industries Ltd.
      PCT Int. Appl., 25 pp.
SO
      CODEN: PIXXD2
DT
      Patent
      English
LA
FAN.CNT 2
      PATENT NO.
                                KIND
                                          DATE
                                                         APPLICATION NO.
                                                                                        DATE
                                                         wo 2006-US916
                                                                                        20060110
PΙ
      wo 2006074478
                                  Α1
                                          20060713
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
                 KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
                MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
                 VN, YU, ZA, ZM, ZW
           RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
                IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
                                                          US 2005-642866P
                                                                                        20050110
                                                          US 2005-690823P
                                                                                    Ρ
                                                                                        20050614
      US 2006194876
                                  A1
                                          20060831
                                                          us 2006-329915
                                                                                        20060110
                                                          US 2005-642866P
                                                                                        20050110
                                                          US 2005-690823P
                                                                                    Ρ
                                                                                        20050614
                                                          us 2006-329922
      us 2006194987
                                          20060831
                                                                                        20060110
                                  Α1
                                                          US 2005-642866P
                                                                                        20050110
                                                          US 2005-690823P
                                                                                        20050614
PATENT FAMILY INFORMATION:
FAN
      2006:677667
      PATENT NO.
                                KIND
                                          DATE
                                                         APPLICATION NO.
                                                                                        DATE
                                 ____
PΙ
      wo 2006074479
                                 Α1
                                          20060713
                                                         wo 2006-US917
                                                                                        20060110
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
                 KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
                MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
                 VN, YU, ZA, ZM, ZW
           RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                KG, KZ, MD, RU, TJ, TM
                                                          US 2005-642866P
                                                                                        20050110
                                                          US 2005-690823P
                                                                                        20050614
      us 2006194876
                                          20060831
                                                          us 2006-329915
                                  Α1
                                                                                        20060110
                                                          US 2005-642866P
                                                                                        20050110
                                                          US 2005-690823P
                                                                                    Р
                                                                                        20050614
                                                         US 2006-329922
US 2005-642866P
                                          20060831
      us 2006194987
                                  A1
                                                                                        20060110
                                                                                    Ρ
                                                                                        20050110
                                                          US 2005-690823P
                                                                                        20050614
                                                                                    Ρ
      The present invention provides substantially pure tolterodine tartrate
AB
      having <0.5% of total impurities, as determined by HPLC, and a pharmaceutical
      composition comprising the substantially pure tolterodine tartrate and at least
      one pharmaceutically acceptable excipient. Thus, a solution was formed by
      combining the N.N-diisopropyl[3-(2-methoxy-5-methylphenyl)-3-
```

phenylpropyl]amine fumarate (200 g, 0.439 mol) and HBr in acetic acid and stirring at about 110 $^\circ$ to 115 $^\circ$ for 14 h. The solution was cooled to room temperature and ice water was added, forming a slurry. The slurry was cooled to 5°, filtered and dried at about 65° under vacuum to yield tolterodine hydrobromide (164.4 g) of 99.26% purity, as determined by HPLC. To a mixture of tolterodine hydrobromide (100 g, 0.246 mol), Et acetate and water at room temperature was added potassium hydroxide (50%, 300 mL). After stirring for approx. 15 to 30 min, two clear homogeneous layers formed. The layers were separated, and an organic phase was obtained. L-tartaric acid (38.33 g) dissolved in ethanol was added in one portion to the organic phase, at room temperature, forming a slurry. The

slurry was cooled to 0° and maintained at this temperature for about 15 h, then it was filtered, washed and dried yielding tolterodine tartrate (62.6 g).

The tolterodine tartrate was recrystd. from dry ethanol yielding tolterodine tartrate (41.2 g) of 99.84% purity, as determined by HPLC.

IT 124937-52-6P, Tolterodine tartrate RL: ANT (Analyte); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substantially pure tolterodine tartrate for dosage forms)

RN

124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

87-69-4 CRN C4 H6 O6 CMF

Absolute stereochemistry.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 9 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2006:627597
                     CAPLUS
AN
DN
      145:103428
      Process for preparation of 3-(2-hydroxy-5-methylphenyl)-N.N-diisopropyl-3-
TI
      phenylpropylamine
IN
      Toplak, Renata
      Lek Pharmaceuticals D.D., Slovenia
PA
      PCT Int. Appl., 36 pp.
S0
      CODEN: PIXXD2
DT
      Patent
      English
LA
FAN.CNT 1
                                                       APPLICATION NO.
                                                                                    DATE
      PATENT NO.
                               KIND
                                        DATE
ΡI
      wo 2006066931
                                Α1
                                        20060629
                                                       WO 2005-EP13899
                                                                                     20051222
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
                KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
                MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
                VN, YU, ZA, ZM, ZW
           RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
                GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                KG, KZ, MD, RU, TJ, TM
                                                       SI 2004-349
                                                                                 A 20041224
OS
      MARPAT 145:103428
      A new process for the preparation of 3-(2-hydroxy-5-methylphenyl)-N,N-
AB
      diisopropyl-3-phenylpropylamine (tolterodine) from 3,4-dihydro-6-methyl-4-
      phenyl-2-benzopyran-2-one is characterized by intermediates such as 3-(2-hydroxy-5-methylphenyl)-3-phenylpropanol (I) and its sulfonated
      derivs. and amination in the presence of sodium iodide. Thus, treatment of I ditosylate with diisopropylamine and deoxygenation with t-BuOK in t-BuOH and deoxygenated deionized water afforded tolterodine, which was
      resolved as the (+)-tartrate.
IT
      124937-52-6P
      RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
      (Preparation)
          (preparation of (hydroxymethylphenyl)diisopropylphenylpropylamine
          (tolterodine))
RN
      124937-52-6 CAPLUS
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
      CRN
            124937-51-5
            C22 H31 N O
      CMF
Absolute stereochemistry. Rotation (+).
```

2 CM

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 5 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

2006:409059 CAPLUS AN

DN 144:412229

TI

Process for preparing high-purity tolterodine
Venkataraman, Sundaram; Mathad, Vijayavitthal Thippannachar; Reddy,
Kikkuru Srinivasan, Neti; Reddy, Chinta Raveendra; Arunagiri, IN Muthulingam; Kumari, Routhu Lalitha

PA India

U.S. Pat. Appl. Publ., 9 pp. SO

CODEN: USXXCO

DT **Patent**

English LA

FAN . CNT

FAIN	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	us 2006094904	A1	20060504	US 2005-259322 US 2004-622829P	20051026

0\$ CASREACT 144:412229

A process for the prepation of high-purity tolterodine comprises reacting Me 3-(2-benzyloxy-5-methylphenyl)-3-phenylpropionate with a reducing agent to form 3-(2-benzyloxy-5-methylphenyl)-3-phenylpropanol. AB

124937-52-6P, Tolterodine tartrate IT

RL: SPN (Synthetic preparation); PREP (Preparation) (in a process for preparing high-purity tolterodine)

124937-52-6 CAPLUS RN

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

124937-51-5 CRN

CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11

```
2006:341629 CAPLUS
ΑN
      144:390558
DN
     Process for the preparation of N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenyl-propaneamine (i.e., racemic tolterodine)
TI
     Turchetta, Stefano; Ciambecchini, Umberto; Massardo, Pietro
IN
PA
     Chemi SpA, Italy
S0
      U.S. Pat. Appl. Publ., 11 pp.
      CODEN: USXXCO
DT
      Patent
      English
LA
FAN.CNT 1
      PATENT NO.
                             KIND
                                     DATE
                                                   APPLICATION NO.
                                                                              DATE
     US 2006079716
                                                                              20051006
PΙ
                              A1
                                     20060413
                                                   us 2005-244396
                                                   IT 2004-MI1920
                                                                            20041011
                                                                          Α
os
     CASREACT 144:390558; MARPAT 144:390558
     A process for the preparation of racemic tolterodine its pharmaceutically
AB
     acceptable salts comprises: substitution of the sulfonyloxy group of the
      compound [I; R = C1-6 alkyl, CH2A, SiR23; A = (un)substituted aryl; R2 =
      (un)branched alkyl, (un)substituted aryl, acyl; and R1 = C1-6 alkyl, (un)substituted aryl] with N,N-diisopropylamine in a solvent comprising an
      ionic liquid to yield the tertiary amine (II); and optionally, salification
     with a pharmaceutically acceptable acid. 124937-52-6P
IT
     RL: PNU (Preparation, unclassified); PREP (Preparation)
         (preparation of)
RN
     124937-52-6 CAPLUS
     Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
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ANSWER 11 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

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(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5

CMF C22 H31 N O
```

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
ANSWER 12 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
     2006:268720 CAPLUS
AN
DN
     144:318487
ΤI
     Biosynchronous transdermal drug delivery
     DiPierro, Guy; Giannos, Steven
IN
     Chrono Therapeutics, Inc., USA
PA
     PCT Int. Appl., 85 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
                            KIND
                                                 APPLICATION NO.
                                                                            DATE
     PATENT NO.
                                    DATE
                             A2
ΡI
     wo 2006031856
                                    20060323
                                                 wo 2005-US32672
                                                                            20050913
     wo 2006031856
                             Α3
                                    20060817
              AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
              IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
```

IT

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

US 2004-609418P P 20040913 US 2005-162517 A 20050913 US 2006062838 A1 20060323 US 2005-162525 20050913 US 2004-609418P P 20040913

AB A delivery mechanism and device for the passive periodic release of a drug or an active ingredient and the methods for synchronizing the administration of compds. with the human body's natural circadian rhythms and addiction rhythms. This strategy is intended to counteract disease states and symptoms when they are likely to be at their worst by using an automated and pre-programmable transdermal or other drug administration system.

124937-52-6, Detrol
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(biosynchronous transdermal drug delivery)

RN 124937-52-6 CAPLUS
CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 13 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN

AN 2006:184347 CAPLUS

DN 144:260801

```
Sustained release pharmaceutical composition of tolterodine
TI
      Kramar, Andrejka; Pisek, Robert; Rajer, Tadeja
IN
      Krka, D.D., Novo Mesto, Slovenia
PA
SO
      Eur. Pat. Appl., 13 pp.
      CODEN: EPXXDW
DT
      Patent
      English
LA
FAN.CNT 1
                               KIND
                                        DATE
                                                      APPLICATION NO.
                                                                                   DATE
      PATENT NO.
                                                                                   20040827
PΙ
      EP 1629834
                                Α1
                                        20060301
                                                      EP 2004-20431
               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, D21425 A1 20060302 WO 2005-EP9102 20050823
      wo 2006021425
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
                LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
                NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
                ZA, ZM, ZW
           RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                KG, KZ, MD, RU, TJ, TM
                                                      EP 2004-20431
                                                                               A . 20040827
      The present invention is directed to a sustained-release pharmaceutical
AB
      composition comprising tolterodine, preferably tolterodine tartrate, to the use
      of said composition for the preparation of a medicament and to a method for
      producing such a sustained release pharmaceutical composition
IT
      124937-52-6, Tolterodine tartrate
      RL: PEP (Physical, engineering or chemical process); PYP (Physical
      process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);
      USES (Uses)
          (sustained-release pharmaceutical composition of tolterodine)
RN
      124937-52-6 CAPLUS
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
            1
      CRN
           124937-51-5
      CMF
           C22 H31 N O
Absolute stereochemistry. Rotation (+).
   ОН
          Ph
                      N(Pr-i)_2
```

CM 2

Me

87-69-4 CRN с4 н6 об CMF

Absolute stereochemistry.

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 4

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ALL CITATIONS AVAILABLE IN THE RE FORMAT
      ANSWER 14 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
      2006:99736 CAPLUS
AN
      144:184692
DN
      Use of compounds active on the sigma receptor for the treatment of
ΤI
      mechanical allodynia
      Baeyens Cabrera, Jose Manuel
Laboratorios Del Dr. Esteve, S.A., Spain
IN
PA
SO
      PCT Int. Appl., 52 pp.
      CODEN: PIXXD2
DT
      Patent
IΑ
      English
FAN.CNT 3
                                                        APPLICATION NO.
                                                                                       DATE
                                KIND
                                         DATE
      PATENT NO.
                                                                                       20050725
                                         20060202
                                                        WO 2005-EP8080
      wo 2006010587
                                 Α1
PΙ
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
                NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
                ZA, ZM, ZW
           RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
                IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
                CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                KG, KZ, MD, RU, TJ, TM
                                                         EP 2004-17561
                                                                                      20040724
                                                        EP 2004-17562
                                                                                       20040724
                                                                                  Α
                                                        us 2004-902272
                                                                                       20040730
                                                                                  Α
                                                        us 2004-902273
                                                                                       20040730
                                                                                  Α
                                                        EP 2004-20376
                                                                                       20040827
      US 2006019968
                                 Α1
                                         20060126
                                                        us 2004-902272
                                                                                       20040730
                                                         EP 2004-17561
                                                                                       20040724
                                                        us 2004-902273
                                                                                       20040730
      us 2006019969
                                 Α1
                                         20060126
                                                        EP 2004-17562
                                                                                      20040724
PATENT FAMILY INFORMATION:
     2006:78510
                                KIND
                                         DATE
                                                        APPLICATION NO.
                                                                                       DATE
      PATENT NO.
      US 2006019969
                                         20060126
                                                        US 2004-902273
                                                                                       20040730
PΙ
                                 Α1
                                                        EP 2004-17562
                                                                                     20040724
                                         20060202
                                                        WO 2005-EP8080
                                                                                      20050725
      wo 2006010587
                                Α1
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
               LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
               NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
               SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
               ZA. ZM. ZW
          RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
               IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
               CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
               KG, KZ, MD, RU, TJ, TM
                                                    EP 2004-17561
                                                                               20040724
                                                       2004-17562
                                                                               20040724
                                                    EΡ
                                                                           Α
                                                   us 2004-902272
                                                                               20040730
                                                                           Α
                                                    us 2004-902273
                                                                               20040730
                                                                           Α
                                                    EP 2004-20376
                                                                               20040827
FAN
      2006:79246
      PATENT NO.
                             KIND
                                     DATE
                                                   APPLICATION NO.
                                                                               DATE
                              Α1
                                     20060126
                                                   US 2004-902272
                                                                               20040730
PI
      US 2006019968
                                                       2004-17561
                                                    EΡ
                                                                               20040724
                                     20060202
                                                   WO 2005-EP8080
                                                                               20050725
      wo 2006010587
                              A1
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
               LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
               NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
               SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
               ZA, ZM, ZW
          RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
               IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
               CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
                                                    EP 2004-17561
                                                                               20040724
                                                    EP 2004-17562
                                                                               20040724
                                                                           Α
                                                   us 2004-902272
                                                                               20040730
                                                                           Α
                                                    US 2004-902273
                                                                               20040730
                                                                           Α
                                                    EP 2004-20376
                                                                               20040827
os
      MARPAT 144:184692
      The invention discloses the use of compds. active on the sigma receptor
AB
      for the treatment of mech. allodynia.
IT
      124937-52-6
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
         (sigma receptor modulators for treatment of mech. allodynia)
      124937-52-6 CAPLUS
RN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R, 3R)-2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
      CRN
           124937-51-5
           C22 H31 N O
      CMF
```

2 CM

87-69-4 CRN C4 H6 O6 CMF

Absolute stereochemistry.

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 6 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 15 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

2006:80185 CAPLUS ΑN

144:128739 DN

Method for preparation of tolterodine tartrate TI

IN Zhao, Zhiquan

PA

Lunan Pharmaceutical Co., Ltd., Peop. Rep. China Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp. S₀

CODEN: CNXXEV

DT **Patent**

Chinese LA

FAN. CNT 1

AB

IAN	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE		
ΡI	CN 1626504	A	20050615	CN 2004-10058502 CN 2004-10058502	20040816 20040816		

os CASREACT 144:128739

This invention pertains to a method for preparation of tolterodine tartrate by condensing trans-cinnamic alc. ester and p-methylphenol in the presence of acid such as inorg. acid of sulfuric acid, hydrochloric acid, nitric acid, phosphoric acid, hydrobromic acid, hydrobromic acid, hydrobromic acid, oxalic acid, benzoic acid, paratolucia acid at 75-146° for 4-25 h, then coupling with diisopropylamine to form racemic tolterodine, optical resolution with L-(+)tartrate to give L-(+)-tartrate-R-tolterodine and coproduct L-(+)-tartrate-S-tolterodine, removing L-(+)tartrate by reacting with inorg. base, transfering S configuration to R, further saltifying R with L-(+)tartrat to obtain L-(+)tartrate-R-tolterodine. Trans-cinnamic alc. ester can be fluoroform sulfonic acid ester, fluoroform acetate, p-nitrobenzoate, 3,5-dinitrobenzoate or 2,4,6-trinitrobenzoate. Thus, 4-methylphenol, trans-cinnamic alc. 3,5-dinitrobenzoate and concentrated sulfuric acid mixed together and heated to 135-138°, stirred for 8 h, then cooled down

and neutralized with 10% sodium hydroxide, extracted with Et acetate, the organic phase washed with 5% potassium carbonate and dried with anhydrous sodium sulfate, after vacuum evaporated solvent and isopropanol recrystn. to give the product 3-(2-hydroxy-5-methylphenyl)-3-phenylproplen-3,5-dinitrobenzoate with vield 82.8%. 124937-52-6P IT RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of optical tolterodine tartrate) RN 124937-52-6 CAPLUS Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME) CN CM CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2 CRN 87-69-4 CMF C4 H6 06

Absolute stereochemistry.

ANSWER 16 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11 2006:38921 CAPLUS AN 144:177457 DN Manufacture of tolterodine tartrate dispersible tablet TI Zhao, Zhiquan IN Lunan Pharmaceutical Co., Ltd., Peop. Rep. China Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp. PA **SO** CODEN: CNXXEV DT Patent Chinese LA FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE

ΡI Α 20050622 CN 2004-10057363 20040830 CN 1628646 CN 2004-10057363 20040830 AB The title dispersible tablet is composed of: tolterodine tartrate as active component, disintegrating agent, and auxiliary additive. This tablet can be used for treating urinary urgency, sychnuria, and urinary incontinence, and has the advantages of high dissoln. rate, high bioavailability, and less adverse effects.

124937-52-6, Tolterodine tartrate IT RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(manufacture of tolterodine tartrate dispersible tablet) 124937-52-6 CAPLUS RN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME) CM 1 124937-51-5 CRN CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 17 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN 2006:11150 CAPLUS AN DN 144:64351 TI Co-administration of dehydroepiandrosterone (dhea) congener with pharmaceutically active agents for treating inflammation Patel, Dinesh; Vollmer, David; Daugherty, Claire; Gebhard, John Inflabloc Pharmaceuticals, Inc., USA IN PA SO U.S. Pat. Appl. Publ., 22 pp. CODEN: USXXCO DT Patent Enalish LA

FAN.CNT 4 PATENT NO. KIND DATE APPLICATION NO. DATE								
ΡI	us 2006004076		US 2005-145024	20050603				
P.I.	wo 2006007312 wo 2006007312	A2 20060119 A3 20060427	US 2004-584350P	P 20040630 20050606				
	W: AE, AG, AI CN, CO, CI GE, GH, GI LC, LK, LI NG, NI, N	AM, AT, AU, AZ, BAR, CU, CZ, DE, DK, DM, HR, HU, ID, IL, IM, LS, LT, LU, LV, MAD, NZ, OM, PG, PH, PI	M, DZ, EC, EE, EG, E N, IS, JP, KE, KG, H A, MD, MG, MK, MN, M L, PT, RO, RU, SC, S	ES, FI, GB, GD, KM, KP, KR, KZ, MW, MX, MZ, NA, SD, SE, SG, SK,				
	RW: AT, BE, B IS, IT, L CG, CI, C	G, CH, CY, CZ, DE, DI F, LU, MC, NL, PL, P ⁻ M, GA, GN, GQ, GW, MI W, MZ, NA, SD, SL, SZ	T, RO, SE, SI, SK, TL, MR, NE, SN, TD, TZ, TZ, UG, ZM, ZW, A	TR, BF, BJ, CF, TG, BW, GH, GM, AM, AZ, BY, KG,				
	US 2006122160	A1 20060608	US 2004-584350P US 2005-145024 US 2005-270326 US 2004-584350P	P 20040630 A 20050603 20051108 P 20040630				
	us 2006154908	A1 20060713	US 2005-145024 US 2006-342276 US 2004-584350P	A2 20050603 20060126 P 20040630				
	us 2006217355	A1 20060928	US 2005-145024 US 2006-370218 US 2004-584350P US 2005-145024	20060306				
PATE FAN	NT FAMILY INFORMAT 2006:544792							
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE				
ΡΙ	us 2006122160	A1 20060608	US 2005-270326 US 2004-584350P US 2005-145024	20051108 P 20040630 A2 20050603				
	us 2006004076	A1 20060105	US 2005-145024 US 2004-584350P	20050603				
FAN	2006:677763 PATENT NO.	KIND DATE	APPLICATION NO.					
ΡI	US 2006154908	A1 20060713	US 2006-342276 US 2004-584350P US 2005-145024	20060126 P 20040630 A2 20050603				
	us 2006004076	A1 20060105	US 2005-145024 US 2005-145024 US 2004-584350P	20050603				
FAN	2006:1012512 PATENT NO.	KIND DATE	APPLICATION NO.	DATE				
ΡI	US 2006217355	A1 20060928	us 2006-370218 us 2004-584350P us 2005-145024	20060306 P 20040630				
	us 2006004076	A1 20060105	US 2005-145024 US 2005-145024 US 2004-584350P	20050603 P 20040630				
AB	dehydroepiandroste invention relates (DHEA) congener in	tion is related to the rone (DHEA) congener to the co-administral combination with attending tartrate	nerapeutic uses of rs. More specifical ation of a dehydroep	lly, the present piandrosterone				

Absolute stereochemistry. Rotation (+).

C22 H31 N O

CM 2

CMF

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 18 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2006:4736 CAPLUS

DN 144:247032

TI Characterization of muscarinic receptor binding and inhibition of salivation after oral administration of tolterodine in mice

AU Oki, Tomomi; Maruyama, Shuji; Takagi, Yukiko; Yamamura, Henry I.; Yamada, Shizuo

CS Department of Pharmacokinetics and Pharmacodynamics and COE Program in the 21st Century, School of Pharmaceutical Science, University of Shizuoka, Suruga-ku. Shizuoka. 422-8526. Japan

Suruga-ku, Śhizuoka, 422-8526, Japan SO European Journal of Pharmacology (2006), 529(1-3), 157-163 CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier B.V.

DT Journal

LA English

AB The current study was undertaken to characterize the effects of oral administration of tolterodine on muscarinic receptor binding in the bladder and submaxillary gland and on salivation in mice. In the in vitro

experiment, tolterodine and its metabolite (5-hydroxymethyl metabolite: 5-HM) competed concentration-dependently with [N-methyl-3H]-scopolamine ([3H]NMS) in the mouse bladder, submaxillary gland and heart, and the potencies of both agents were greater than that of oxybutynin. After oral administration of tolterodine (6.31, 21.0 \(mol/kg)\) and oxybutynin (76.1 \(mol/kg)\), there was a dose and time-dependent increase in Kd values for specific [3H]NMS binding in the bladder, prostate, submaxillary gland, heart, colon and lung, compared with control values, suggesting significant muscarinic receptor binding in each tissue. The Kd increase in each tissue by oral oxybutynin reached a maximum value of 0.5 h after oral administration and then rapidly declined, while that by tolterodine was greatest 2 h after the administration and it was maintained for at least 6 or 12 h, depending on the dose and on the tissue. Thus, muscarinic receptor binding of oral tolterodine was slower in onset and of a longer duration than that of oxybutynin. Also, oral oxybutynin showed relatively greater receptor binding in the submaxillary gland as compared with other tissues, but such binding in the submaxillary gland as compared with other tissues, but such high selectivity to the exocrine gland muscarinic receptors was not observed by oral tolterodine. Oral administration of tolterodine and oxybutynin reduced significantly the pilocarpine-induced salivary secretion in mice, and the attenuation of oral tolterodine appeared more slowly and it was more persistent than that of oral oxybutynin. The antagonistic effect of oral tolterodine on the dose-response curves to pilocarpine was significantly weaker than that of oxybutynin. These data suggest that oral tolterodine, compared with the case of oral oxybutynin, binds more selectively to muscarinic receptors in the mouse bladder than in the submaxillary gland, which may be advantageous in treating patients with overactive bladder.

124937-52-6, Tolterodine tartrate IT

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(characterization of muscarinic receptor binding and inhibition of

salivation after oral administration of tolterodine in mice)

RN

124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM

CN

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

CRN **67-69-4** CMF C4 H6 O6

Absolute stereochemistry.

```
RE.CNT 22
                    THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
                    ALL CITATIONS AVAILABLE IN THE RE FORMAT
L11
       ANSWER 19 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
        2005:1220192 CAPLUS
ΑN
        143:466219
DN
        Permeation enhancing compositions for anticholinergic agents containing
TI
       urea compounds
       Grenier, Arnaud; Carrara, Dario Norberto R.; Besse, Celine
IN
PA
       Antares Pharma Ipl A.-G., Switz.
       PCT Int. Appl., 70 pp.
S<sub>0</sub>
       CODEN: PIXXD2
DT
       Patent
       English
LA
FAN.CNT 1
       PATENT NO.
                                    KIND
                                               DATE
                                                                APPLICATION NO.
                                                                                                   DATE
PΙ
       wo 2005107812
                                      Α1
                                               20051117
                                                                WO 2005-EP4799
                                                                                                   20050503
                   AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                  CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
                   ZM, ZW
             RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
                   AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
                   EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
                   RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
                   MR, NE, SN, TD, TG
                                                                US 2004-568983P
                                                                                                   20040507
                                                                US 2005-120306
       US 2005287194
                                               20051229
                                                                                                   20050502
                                      Α1
                                                                US 2004-568983P
                                                                                                  20040507
os
       MARPAT 143:466219
       A transdermal or topical composition including anticholinergic agents, such as oxybutynin, a urea-containing compound and a carrier system. A method is
AB
       disclosed for treating a subject for urinary incontinence while reducing the incidences of peak concess of drug and undesirable side effects. For
       example, gel containing oxybutynin 3, ethanol 50.72, diethylene glycol monoethyl ether 2.5, propylene glycol 15, urea 5, Klucel MF 2, butylhydroxytoluene 0.05%, was found to have a better pharmacokinetic and permeation character than the gel without urea.
IT
       124937-52-6
       RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
```

(transdermal and topical compns. containing anticholinergics and antispasmodic agents and urea compound for improved permeation)

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,

(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

Page 37

CM

1

RN

CN

124937-52-6 CAPLUS

124937-51-5 CRN CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 6 ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 20 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
```

AN 2005:1193308 CAPLUS

DN 143:466159

Controlled release mucoadhesive matrix formulation containing tolterodine TI and a process for its preparation

Durga Maheswari, Parvataneni; Appalaswamy Naidu, Rongala; Podile, Khadgapathi; Venkaiah Chowdary, Nannapaneni Natco Pharma Limited, India IN

PA

PCT Int. Appl., 36 pp. SO

CODEN: PIXXD2

DT Patent

English LA

FAN.	.CNT I			
	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
ΡI	wo 2005105036	A1 20051110	wo 2005-IN99	20050404
	W: AE, AG, AL,	, AM, AT, AU, AZ,	BA, BB, BG, BR, BW, BY,	BZ, CA, CH,
	CN, CO, CR,	CU, CZ, DE, DK,	DM, DZ, EC, EE, EG, ES,	FI, GB, GD,
	GE, GH, GM,	, HR, HU, ID, IL,	IN, IS, JP, KE, KG, KM,	KP, KR, KZ,
			MA, MD, MG, MK, MN, MW,	
	NI, NO, NZ,	OM, PG, PH, PL,	PT, RO, RU, SC, SD, SE,	SG, SK, SL,
	SM, SY, TJ,	TM, TN, TR, TT,	TZ, UA, UG, US, UZ, VC,	VN, YU, ZA,
	ZM, ZW			
			NA, SD, SL, SZ, TZ, UG,	
	AZ. BY. KG.	. KZ. MD. RU. TJ.	·TM. AT. BE. BG. CH. CY.	CZ. DE. DK.

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IN 2004-CH393 A 20040428

Controlled release oral pharmaceutical mucoadhesive matrix formulation containing a therapeutically effective amount of tolterodine or its pharmaceutically acceptable salts, prodrugs and metabolites thereof dispersed in a rate controlling polymeric matrix comprising (1) a pH independent gelling polymer, such as polyethylene oxide, (2) pH dependent gelling polymer, such as sodium CM-cellulose (3) a film coating polymer component, such as Eudragit RS100 and other conventional tablet functional excipients. The formulation such as tablets or minitablets in capsules of the present invention relates to a 24 h controlled release dosage form useful for the treatment of urge incontinence and other symptoms of unstable or overactive urinary bladder. The invention also relates to a process for the preparation of controlled release mucoadhesive matrix formulation containing tolterodine in a tablet or mini tablets in capsule dosage form. For example, controlled-release mucoadhesive matrix tablets were prepared by wet granulation of tolterodine tartrate 2.0, polyethylene oxide-18 NF 7.0, sodium CM-cellulose 3.0, lactose anhydrous 20.0, microcryst. cellulose 51.8, polyvinylpyrrolidone K-30 5.0, Eudragit RS 100 10.0, iso-Pr alc. 72, and acetone 48, granules obtained were dried, lubricated with colloidal silica 0.1, talc 0.1, and magnesium stearate 1.0 mg, resp., and compressed into core tablets. Eudragit L 100-55 3.0 was added to a mixture of iso-Pr alc. 25.6 and acetone 37.8, followed by tri-Et citrate 0.5 mg, resp., and the solution obtained was used as a barrier coating for core tablets.

IT 124937-52-6, Tolterodine tartrate
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES

(preparation of controlled-release polymeric mucoadhesive matrix containing tolterodine for tablets or minitablets)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 21 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11 2005:1179331 CAPLUS AN 143:393317 DN New spectrophotometric methods for the estimation of tolterodine tartrate TI in pharmaceutical formulations Sankar, D. Gowri; Kumar, D. V. S. P.; Krishna, M. Vamsi; Latha, P. V. M. ΑU Department of Pharmaceutical Science, Andhra University, Visakhapatnam, CS 530 003, India Asian Journal of Chemistry (2005), 17(2), 1357-1359 CODEN: AJCHEW; ISSN: 0970-7077 SO Asian Journal of Chemistry DT Journal English LA Two simple and sensitive visible spectrophotometric methods (methods A and AB B) were developed for the estimation of tolterodine tartrate in pure as well as in pharmaceutical formulations. Method A is based on the oxidative coupling reaction with 3-methyl-2-benzothiazolinone hydrazone (MBTH) in the presence of ceric ammonium sulfate (CAS) to form a colored species with λ max at 555 nm. Method B is based on the oxidation of the drug with ferric chloride followed by complexation with 1,10-phenanthroline (1,10-PTL) to form a blood red colored chromogen with λ max at 520 nm. Beer's law is obeyed in the range of 10-50 and 2.5- 12.5 μ g/mL for methods A and B resp. The results obtained are reproducible and statistically validated and also found to be suitable for the assay of tolterodine tartrate in bulk as well as in pharmaceutical formulations. 124937-52-6, Tolterodine tartrate IT RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (spectrophotometric estimation of tolterodine tartrate in pharmaceutical formulations) 124937-52-6 CAPLUS RN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME) CM 1

Absolute stereochemistry. Rotation (+).

124937-51-5

C22 H31 N O

CRN CMF

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 22 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
     2005:1171039 CAPLUS
AN
     143:411108
DN
     Pharmaceutical compositions containing phosphodiesterase IV-inhibiting
TI
     benzofuran derivative and anticholinergics
     Abe, Yuzuru; Yoshimatsu, Akiko; Miki, Ichiro
Kyowa Hakko Kogyo Co., Ltd., Japan
IN
PA
     PCT Int. Appl., 39 pp.
S0
     CODEN: PIXXD2
DT
     Patent
LA
     Japanese
FAN.CNT 1
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DATE
       PATENT NO.
                                   KIND
                                             DATE
                                                              APPLICATION NO.
      wo 2005102344
                                                                                              20050427
ΡI
                                             20051103
                                                              WO 2005-JP7966
                                    Α1
                  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                  CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
                  SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
            RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
                  AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
                  EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
                  RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
```

JP 2004-131880 A 20040427

AB Disclosed is a pharmaceutical composition containing (a) 4-[(3,5-dichloro-4-pyridyl)carbamoyl]-7-methoxy-2-(4-methylpiperazine-1-ylcarbonyl)benzofuran(I) or a pharmacol. acceptable salt thereof and (b)

an anticholinergic agent. Also disclosed is such a pharmaceutical composition wherein the anticholinergic agent is a compound selected from the group consisting of tiotropium, ipratropium, oxitropium, tolterodine and oxybutynin, or a pharmacol. acceptable salt thereof. The compns. The compns. are effective for the treatment of chronic obstructive pulmonary disease and asthma. For example, a tablet was formulated containing I 20, tolterodine tartrate 2, lactose 143, starch 28, hydroxypropyl cellulose 6, and Mg stearate 1 mg/tablet.

IT

124937-52-6, Tolterodine tartrate RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical compns. containing phosphodiesterase IV-inhibiting benzofuran derivative and anticholinergics)

124937-52-6 CAPLUS RN

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

87-69-4 CRN CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 23 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

2005:1051779 CAPLUS ΑN

143:312243 DN

UV spectrophotometric determination of tolterodine tartrate and cefepime TI ΑU

Sankar, D. Gowri; Krishna, M. Vamsi; Kumar, D. V. S. P.; Latha, P. V. M. Department of Pharmaceutical Sciences, Andhra University, Visakhapatnam, CS

530 003, India

SO Asian Journal of Chemistry (2005), 17(3), 2028-2030 CODEN: AJCHEW; ISSN: 0970-7077

PB Asian Journal of Chemistry

DT Journal LA English

AB UV spectrophotometric methods were developed for the determination of tolterodine

tartrate and cefepime in pure and pharmaceutical formulations. These methods obey Beer's law limits in the concentration range of 10-90 and 5-40 $\mu g/mL$, exhibiting maximum absorption at 280 and 240 nm resp. These methods are extended to pharmaceutical prepns. and there is no interference from any common pharmaceutical additives and diluents. The methods were statistically evaluated and are found to be precise and accurate.

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 24 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN AN 2005:978476 CAPLUS

Page 44 DN 143:259408 High performance liquid chromatography-electrospray ionization mass TI spectrometric determination of tolterodine tartrate in human plasma Zhang, Beibei; Zhang, Zunjian; Tian, Yuan; Xu, Fengguo ΑU Center for Instrumental Analysis, China Pharmaceutical University, CS Jiangsu, 210009, Peop. Rep. China Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2005), 824(1-2), 92-98 50 CODEN: JCBAAI; ISSN: 1570-0232 PΒ Elsevier B.V. DT Journal English LΑ A selective and sensitive high performance liquid chromatog.-electrospray AΒ ionization mass spectrometry (HPLC-ESIMS) method has been developed for the determination of tolterodine tartrate in human plasma. With oxybutynin as internal standard, tolterodine tartrate was extracted from plasma with residue

isopropanol (95:5, volume/volume). The organic layer was evaporated and the

was redissolved in mobile phase comprised of acetonitrile-water (10 mM CH3COONH4, pH 3.0) = 50:50 (volume/volume). An aliquot of 10 μ l was chromatog. analyzed on a prepacked Shimadzu Shim-pack VP-ODS C18 column (150 mm + 2.0 mm I.D.) by means of selected-ion monitoring (SIM) mode mass spectrometry. Standard curves were linear (r = 0.9993) over the concentration range of 0.1-30.0 ng/mL and had good accuracy and precision. The within- and between-batch precisions were within 10% relative standard The limit of detection (LOD) was 0.05 ng/mL. The validated HPLC-ESIMS method has been used successfully to study tolterodine tartrate pharmacokinetic, bioavailability and bioequivalence in 20 healthy male volunteers

124937-52-6, Tolterodine tartrate IT RL: ANT (Analyte); BSU (Biological study, unclassified); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study) (tolterodine tartrate HPLC-ESIMS determination in human plasma)

124937-52-6 CAPLUS RN

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R, 3R) - 2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

87-69-4 CRN C4 H6 O6 CMF

Absolute stereochemistry.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 25 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN
L11
AN
       2005:970635 CAPLUS
DN
       143:415557
       Effect of the proton pump inhibitor omeprazole on the pharmacokinetics of
TI
       extended-release formulations of oxybutynin and tolterodine
       Dmochowski, Roger; Chen, Andrew; Sathyan, Gayatri; MacDiarmid, Scott; Gidwani, Shalini; Gupta, Suneel
Department of Urology, Vanderbilt University School of Medicine,
ΑU
       Nashville, TN, USA
Journal of Clinical Pharmacology (2005), 45(8), 961-968
50
       CODEN: JCPCBR; ISSN: 0091-2700
PB
       Sage Publications
       Journal
DT
       English
LA
       This study assessed the effect of the proton pump inhibitor omeprazole on
the bioavailability of the extended-release formulations of oxybutynin and
AB
       tolterodine. Forty-four healthy volunteers received each of 4 treatments in a 4-period crossover design. The treatments consisted of osmotically controlled extended-release oxybutynin chloride tablets at 10 mg/d or extended-release tolterodine tartrate capsules at 4 mg/d, with and without
       preceding treatment with 20 mg omeprazole daily for 4 days. Blood samples collected predose and at scheduled time points for 36 h postdose were
       analyzed for oxybutynin and its active metabolite, N-desethyloxybutynin,
       or tolterodine and its active 5-hydroxymethyl metabolite, as appropriate.
       The AUC∞ ratios for oxybutynin and its metabolite with and without
       prior omeprazole fell within the 80% to 125% range (accepted as the
       criterion for bioequivalence), as did those for tolterodine and its active
                   The peak concentration ratios for oxybutynin and metabolite also
      conformed to this range; those for tolterodine did not. Increasing gastric pH with omeprazole does not substantially alter the pharmacokinetic properties of extended-release oxybutynin but may alter those of extended-release tolterodine.

124937-52-6, Tolterodine tartrate
IT
       RL: PKT (Phármacokinetics); THU (Therapeutic use); BIOL (Biological
       study): USES (Uses)
           (pharmacokinetic properties were altered for extended release
           tolterodine proton pump inhibitor omeprazole with greater Cmax in
       124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
RN
CN
       (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
       CM
              1
             124937-51-5
       CRN
             C22 H31 N O
       CMF
```

Page 46

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF с4 н6 о6

Absolute stereochemistry.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L11
     ANSWER 26 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
     2005:638702 CAPLUS
ΑN
     143:139193
DN
     Novel pharmaceutical compositions
ΤI
     Gupta, Vinod Kumar; Vaya, Navin
IN
     Torrent Pharmaceuticals Limited, India
PA
     PCT Int. Appl., 37 pp.
S0
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                             APPLICATION NO.
PΙ
     wo 2005065639
                          Α2
                                20050721
                                             WO 2004-IN321
     wo 2005065639
                          Α3
                                20050901
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             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

DATE

20041018

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

IN 2003-MU1201 A 20031121 A dosage form comprising of an active ingredient as modified release and AB an active ingredient as immediate release. Wherein the modified release

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active ingredient is selected from high dose, low solubility active ingredients
     or low dose, low solubility active ingredients or low dose, high solubility
active
     ingredients and the immediate release active ingredient is selected from
     low dose active ingredients. Thus, tablets were obtained from
     nebivolol-HCl 6.1, lactose monohydrate 78.5, red ferric oxide 0.6, and PVP
     K30 3.3%.
     124937-52-6, Tolterodinetartrate
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (pharmaceutical compns.)
     124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
RN
     CM
           124937-51-5
     CRN
          C22 H31 N O
```

Absolute stereochemistry. Rotation (+).

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
L11
    ANSWER 27 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
     2005:588860 CAPLUS
AN
DN
     143:115342
     A preparation of tolterodine and its salts with improved purity, useful as
TI
     anticholinergic agent
     Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
IN
PA
     Cipla Limited, India; Wain, Christopher Paul
SO
     PCT Int. Appl., 32 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
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DATE
                                                        APPLICATION NO.
      PATENT NO.
                                KIND
                                         DATE
PΙ
      wo 2005061432
                                 Α1
                                         20050707
                                                        WO 2004-GB5420
                                                                                      20041223
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
                LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
                NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
           TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG
                                                        GB 2003-30056
                                                                                     20031224
                                                        GB 2004-23300
                                                                                     20041020
      CA 2551501
                                 AA
                                         20050707
                                                        CA 2004-2551501
                                                                                      20041223
                                                        GB 2003-30056
                                                                                     20031224
                                                        GB 2004-23300
                                                                                     20041020
                                                                                 Δ
                                                        WO 2004-GB5420
                                                                                 W
                                                                                     20041223
      EP 1701932
                                         20060920
                                                        EP 2004-820622
                                                                                      20041223
                                 Α1
                AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

GB 2003-30056 A 20031224
                                                                                     20041020
                                                        GB 2004-23300
                                                        WO 2004-GB5420
                                                                                     20041223
os
      CASREACT 143:115342
      The invention relates to a preparation of (+)-tolterodine (I) and its salts
AΒ
      with improved purity, useful as anticholinergic agent (no data).
      of I was prepared via amination of the prepared sulfonic acid ester II by
      diisopropylamine, hydrolysis, purification, and salt formation. Dimeric
      impurity associated with tolterodine tartrate was measured (< 0.1%).
IT
      124937-52-6P, Tolterodine tartrate
      RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
          (preparation of tolterodine and its salts with improved purity useful as
          anticholinergic agent)
RN
      124937-52-6 CAPLUS
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
            1
      CRN
            124937-51-5
      CMF
            C22 H31 N O
```

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 28 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
      2005:588858 CAPLUS
DN
      143:115346
      Improved process for the industrial preparation of tolterodine via
TI
      reductive amination of an aldehyde intermediate
Pascual Coca, Gustavo; Martin Pascual, Pablo; Martin Juarez, Jorge
IN
      Ragactives, S.L., Spain PCT Int. Appl., 31 pp.
PA
S0
      CODEN: PIXXD2
DT
      Patent
      Spanish
LA
FAN.CNT 1
      PATENT NO.
                              KIND
                                       DATE
                                                      APPLICATION NO.
                                                                                   DATE
                               Α1
                                       20050707
                                                      WO 2004-ES572
                                                                                   20041221
PΙ
      wo 2005061431
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
               CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
                TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
           RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
                AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
                EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
                RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
                MR, NE, SN, TD, TG
                                                      ES 2003-3032
                                                                               A 20031222
      ES 2235648
                                                      ES 2003-3032
CA 2004-2550477
                                       20050701
                                                                                   20031222
                                Α1
      CA 2550477
                                AA
                                       20050707
                                                                                   20041221
                                                      ES 2003-3032
                                                                                   20031222
                                                      WO 2004-ES572
                                                                                   20041221
                                                                               W
      EP 1698615
                                       20060906
                                                      EP 2004-805115
                                                                                   20041221
                               Α1
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS
                                                      ES 2003-3032
                                                                               A 20031222
                                                      WO 2004-ES572
                                                                                  20041221
      CASREACT 143:115346; MARPAT 143:115346
OS
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AB The invention relates to a method of obtaining tolterodine (I). The inventive method consists in: (1) reacting an aldehyde II (R = protective group for hydroxyl) with HN(Pr-iso)2 in the presence of a reducing agent; (2) optionally converting the resulting amine intermediate III into a salt, and, if desired, isolating it; (3) removing the hydroxyl protective group to give I; and (4) if desired, separating the desired (R) or (S) enantiomer (or their mixture), and/or converting the compound thus obtained

into a pharmaceutically acceptable salt. I is a known muscarinic receptor antagonist (no data) which can be used in the treatment of urinary incontinence and other symptoms of urinary bladder hyperactivity. The new process is designed to be more economical, to use less dangerous reagents, to give better quality product, and to be more productive than known methods, thereby making it more suitable for use on an industrial scale. For instance, Friedel-Crafts acylation of 4-Mec6H4OMe by PhCOCl using SnCl4 gave 78% 2-methoxy-5-methylbenzophenone. Reduction of this ketone using 2 equiv NaBH4 and BF3.THF gave 93% of the corresponding diphenylmethane derivative, which was lithiated with BuLi and ethoxylated with ethylene oxide to give 3-(2-methoxy-5-methylphenyl)-3-phenylpropan-1-ol. Oxidation of this alc. by 4 different oxidizing agents gave II (R = Me); in particular, Swern oxidation with DMSO and oxalyl chloride gave 94% yield. Reductive amination of II (R = Me) with NaBH(OAc)3 and HN(Pr-iso)2 gave 91% III (R = Me), which was treated with HBr in refluxing AcOH to give 64% I.HBr. Addition of the phase-transfer catalyst Bu4N+Br- to the latter demethylation reaction increased the yield to 80%. Alternatively, III (R = Me) was isolated as the HBr salt before demethylation, and was thereby obtained as a crystalline product which was free of impurities. Finally, I.HBr was converted to the (R)-(+)-isomer L-tartrate salt, which was obtained with a purity of 99.80%.

IT 124937-52-6P, (R)-Tolterodine (L)-tartrate
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN
(Synthetic preparation); PREP (Preparation)

(improved preparation of tolterodine via reductive amination of an aldehyde intermediate)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 29 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11 2005:555075 CAPLUS AN 143:359890 DN Extended-release formulations of oxybutynin and tolterodine exhibit TI similar central nervous system tolerability profiles: A subanalysis of data from the OPERA trial Chu, Franklin M.; Dmochowski, Roger R.; Lama, Daniel J.; Anderson, Rodney ΑU U.; Sand, Peter K. CS San Bernardino Urological Associates, San Bernardino, CA, USA American Journal of Obstetrics and Gynecology (2005), 192(6), 1849-1854 SO CODEN: AJOGAH; ISSN: 0002-9378 PB Elsevier Journal DT English LA Objective: This study was undertaken to compare the central nervous system AB (CNS) tolerability profiles of the extended-release formulations of oxybutynin chloride and tolterodine tartrate in the treatment of women with overactive bladder (OAB), as observed in the OPERA (Overactive bladder: Performance of Extended Release Agents) trial. Study design: The OPERA trial was a randomized, double-blind, active-control comparison of the efficacy and safety of extended-release oxybutynin (10 mg/d) and extended-release tolterodine (4 mg/d) given to 790 women with OAB for 12 wk. The incidence of reported CNS events was compared between the treatment groups by using the Fisher exact test. Results: The incidence of CNS adverse events was 9% and 8% for the oxybutynin and tolterodine treatment groups, resp. The difference between groups was not statistically significant. All reported CNS adverse events were rated as mild or moderate in severity. There were no serious treatment-related adverse events in either group, and discontinuation because of a CNS adverse event was infrequent. Conclusion: The extended-release formulations of oxybutynin and tolterodine were observed to be associated with а similar low incidence of CNS adverse events, which were mostly mild or moderate in severity. IT 124937-52-6, Tolterodine tartrate RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (extended release formulation of tolterodine tartrate with CNS adverse event like somnolence, hypertonia and tremor and vertigo had tolerability similar to that of oxybutynin chloride in female patient with overactive bladder) 124937-52-6 CAPLUS RN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN

(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 25 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 30 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

2005:500489 CAPLUS ΑN

143:373118 DN

Tolterodine tartrate sustained-release tablets TI

ΑU

Liu, Zhenghe; Zhang, Junshou; Cao, Deshan Nanjing Meirui-pharma Co., LTD., Nanjing, Jiangsu Province, 210038, Peop. CS Rep. China

S₀ Zhongguo Shenghua Yaowu Zazhi (2004), 25(4), 230-232 CODEN: ZSYZFP; ISSN: 1005-1678

PB Zhongguo Shenghua Yaowu Zazhi Bianjibu

DT Journal

Chinese 1 A

Tolterodine tartrate sustained-release tablets were prepared, and the content of tolterodine tartrate was determined by high performance liquid chromatog. (HPLC). Orthogonal design was employed to establish the relationship between the match-ratio of hydroxypropyl methylcellulose (HPMC) to polyvinylpyrrolidone (PVP) and the release rate in vitro. The AB optimal formulation of tolterodine tartrate sustained-release tablets was as follows: tolterodine tartrate 4 g, HPMC 20 g, mannitol 20 g, dextrin 75 g, 20% PVP and magnesium stearate 2 g. The accumulated release amount of tolterodine tartrate sustained-release tablets was more than 75% within 8 h. HPMC and PVP manufactured by domestic companies can be used properly as barriers to prepare matrix sustained-release tablets of tolterodine The formulation and technique are feasible in industry.

124937-52-6, Tolterodine tartrate IT RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tolterodine tartrate sustained-release tablets)

124937-52-6 CAPLUS RN

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
ANSWER 31 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
       2005:493508 CAPLUS
ΑN
       143:20045
DN
       Use of (+)-isopropyl 2-methoxyethyl 4-(2-chloro-3-cyanophenyl)-1,4-dihydro-
TI
       2,6-dimethylpyridine-3,5-dicarboxylate for the treatment of memory
IN
       Unterbeck, Axel; De Vivo, Michael; Rose, Gregory M.
PA
       Memory Pharmaceuticals Corporation, USA
       PCT Int. Appl., 18 pp.
SO
       CODEN: PIXXD2
DT
       Patent
      English
LA
FAN.CNT 2
       PATENT NO.
                                  KIND
                                            DATE
                                                            APPLICATION NO.
                                                                                            DATE
                                            20050609
      WO 2005051389
                                                                                            20041119
PΙ
                                                            wo 2004-us38624
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                 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

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AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
                NE, SN, TD, TG
                                                       US 2003-523664P
                                                                                    20031121
                                                                                 Ρ
                                                                                    20040909
                                                       US 2004-608116P
      AU 2004292967
                                 Α2
                                        20050609
                                                       AU 2004-292967
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      AU 2004292967
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                                                       US 2004-608116P
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                                                       wo 2004-US38624
                                                                                    20041119
                                                       CA 2004-2546366
                                                                                     20041119
      CA 2546366
                                        20050609
                                 AA
                                                       US 2003-523664P
                                                                                    20031121
                                                                                    20040909
                                                       US 2004-608116P
                                                                                 P
                                                       WO 2004-US38624
                                                                                    20041119
                                                                                W
                                        20050714
                                                       us 2004-992464
                                                                                    20041119
      us 2005153953
                                A1
                                                       US 2003-523664P
                                                                                    20031121
                                                       US 2004-608116P
                                                                                    20040909
                                                                                    20041119
      EP 1684755
                                        20060802
                                                       EP 2004-811352
                                Α1
                AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS US 2003-523664P
                                                                                    20031121
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                                                                                    20040909
                                                       wo 2004-US38624
                                                                                    20041119
PATENT FAMILY INFORMATION:
      2005:493523
FAN
      PATENT NO.
                                                       APPLICATION NO.
                                                                                    DATE
                               KIND
                                        DATE
PΙ
      wo 2005051426
                                A1 -
                                        20050609
                                                       wo 2004-us38623
                                                                                    20041119
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                CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
                LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
           NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
                SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
                NE, SN, TD, TG
                                                       US 2003-523664P
                                                                                    20031121
                                                       US 2004-608116P
                                                                                    20040909
      AU 2004292966
                                A1
                                        20050609
                                                       AU 2004-292966
                                                                                    20041119
                                                       US 2003-523664P
                                                                                Р
                                                                                    20031121
                                                       US 2004-608116P
                                                                                Р
                                                                                    20040909
                                                       wo 2004-us38623
                                                                                    20041119
      CA 2546395
                                AA
                                        20050609
                                                       CA 2004-2546395
                                                                                    20041119
                                                       US 2003-523664P
                                                                                    20031121
                                                       US 2004-608116P
                                                                                Ρ
                                                                                    20040909
                                                       wo 2004-US38623
                                                                                    20041119
      US 2005153953
                                        20050714
                                                       us 2004-992464
                                A1
                                                                                    20041119
                                                       US 2003-523664P
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                                                       US 2004-608116P
                                                                                    20040909
                                        20060802
                                                       EP 2004-811351
      EP 1684806
                                Α1
                                                                                    20041119
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS US 2003-523664P
                                                                                    20031121
                                                       US 2004-608116P
WO 2004-US38623
                                                                                Ρ
                                                                                    20040909
                                                                                W
                                                                                    20041119
      The invention discloses methods for treatment of memory disorders using
AB
      (+)-iso-Pr 2-methoxyethyl 4-(2-chloro-3-cyanophenyl)-1,4-dihydro-2,6-
```

Absolute stereochemistry. Rotation (+).

CM 2 CRN 87-69-4

Absolute stereochemistry.

CMF C4 H6 06

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 32 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11 2005:380709 CAPLUS AN DN 143:77978 Rhodium-Catalyzed Asymmetric 1,4-Addition of Arylboronic Acids to TI Coumarins: Asymmetric Synthesis of (R)-Tolterodine Chen, Gang; Tokunaga, Norihito; Hayashi, Tamio Department of Chemistry, Graduate School of Science, Kyoto University, ΑU CS Kyoto, 606-8502, Japan Organic Letters (2005), 7(11), 2285-2288 CODEN: ORLEF7; ISSN: 1523-7060 American Chemical Society SO PB Journal DT English LA

OS CASREACT 143:77978

AB Rhodium-catalyzed asym. 1,4-addition of arylboronic acids R1B(OH)2 (R1 = Ph, 4-MeC6H4, 3-MeC6H4, 4-ClC6H44, 4-MeOC6H4) to coumarins I (R = 6-Me, H, 6-MeO2C, 8-MeO) proceeded with high enantioselectivity in the presence of a rhodium catalyst (3 mol %) generated from Rh(acac)(C2H4)2 and (R)-segphos to give the corresponding (R)-4-arylchroman-2-ones II in over 99% ee. This asym. reaction was applied to the synthesis of (R)-tolterodine.

IT 124937-52-6P

RL: SPN (Synthetic preparation); PREP (Preparation) (rhodium-catalyzed asym. 1,4-addition of arylboronic acids to coumarins and application to asym. synthesis of (R)-tolterodine)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 06

Absolute stereochemistry.

RE.CNT 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 33 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:358491 CAPLUS

DN 143:61722

An Improved, Scalable, and Impurity-Free Process for Tolterodine Tartrate

AU Srinivas, Keesari; Srinivasan, Neti; Reddy, Kikkuru Srirami; Ramakrishna,

Muddasani; Reddy, Chinta Raveendra; Arunagiri, Muthulingam; Kumari, Routhu

Lalitha; Venkataraman, Sundaraman, Vijagyavitha Tarabata, Toldasa Boyalamana

CS Department of Research and Development, Integrated Product Development,

Page 57

Dr. Reddy's Laboratories Ltd., Bollaram, Jinnaram, Medak District, 502-325, India

SO Organic Process Research & Development (2005), 9(3), 314-318 CODEN: OPRDFK; ISSN: 1083-6160

PB American Chemical Society

DT Journal

LA English

OS CASREACT 143:61722

AB Tolterodine tartrate is an anticholinergic muscle relaxant used to treat urinary frequency, urinary urgency, and incontinence. An improved, cost-effective, and impurity-free process for tolterodine tartrate suitable for large-scale com. production is described with focus on various

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 34 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN AN 2005:185350 CAPLUS

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DN
      143:106714
      Tolterodinium (+)-(2R,3R)-hydrogen tartrate
TI
      Kosutic-Hulita, Nada; Zegarac, Miroslav
Prilaz baruna Filipovica 29, PLIVA Research and Development Ltd, Zagreb,
ΑU
CS
      HR-10000, Croatia
      Acta Crystallographica, Section C: Crystal Structure Communications
SO
      (2005), C61(3), o171-o173
CODEN: ACSCEE; ISSN: 0108-2701
Blackwell Publishing Ltd.
PB
DT
      Journal
LA
      Enalish
      In the crystal structure of (R)-N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropylaminium (2R,3R)-H_tartrate,
AB
      C22H32NO+ C4H5O6-, the H tartrate anions are linked by
      O-H···O H bonds to form helical chains built from
      R22(9) rings. These chains are linked by the tolterodine mols. via
      N-H\cdots O and O-H\cdots O H bonds to
      form sep. sheets parallel to the (101) plane. Crystallog. data are given.
      124937-52-6, Tolterodinium (+)-(2R,3R)-hydrogen tartrate (1:1)
IT
      RL: PRP (Properties)
          (crystal structure of)
      124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
RN
CN
      CM
             1
            124937-51-5
      CRN
      CMF C22 H31 N O
```

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 35 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2005:71091 CAPLUS
AN
      142:162623
DN
      Medicinal compositions containing tricyclic heterocyclic compound and
TT
      anticholinergic agent
      Yamagata, Tsūyoshi; Shirakura, Shiro
IN
      Kyowa Hakko Kógyo Co., Ltd., Japan
PΑ
S0
      PCT Int. Appl., 31 pp.
      CODEN: PIXXD2
DT
      Patent
      Japanese
LA
FAN.CNT 1
      PATENT NO.
                              KIND
                                       DATE
                                                     APPLICATION NO.
                                                                                  DATE
      wo 2005007191
                               Α1
                                       20050127
                                                     WO 2004-JP10521
                                                                                  20040716
PΙ
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
                GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
                LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
                NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
          TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
                SN, TD, TG
                                                      JP 2003-197662
                                                                                  20030716
      CA 2532805
                               AA
                                       20050127
                                                      CA 2004-2532805
                                                                                  20040716
                                                      JP 2003-197662
                                                                                  20030716
                                                     WO 2004-JP10521
                                                                              W
                                                                                  20040716
                                       20060503
                                                                                  20040716
                                                     EP 2004-747885
      EP 1652532
                               A1
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SI
JP 2003-197662
                                                                     SK
                                                                                  20030716
                                                     WO 2004-JP10521
                                                                                  20040716
                                                                              W
                                                     US 2005-562635
                                                                                  20051229
      us 2006160887
                               Α1
                                       20060720
                                                     JP 2003-197662
                                                                                  20030716
                                                     WO 2004-JP10521
                                                                                 20040716
AB
      It is intended to provide a medicinal composition useful in treating, for
      example, hyperactive bladder which comprises 3,3,3-trifluoro-2-hydroxy-2-methyl-N-(5,5,10-trioxo-4,10-dihydrothieno[3,2-c][1]benzothiepin-9-
      yl)propanamide or a pharmacol. acceptable salt thereof and an anticholine
      drug. The effect of combination of (S)-(+)-3,3,3-trifluoro-2-hydroxy-2-methyl-N-(5,5,10-trioxo-4,10-dihydrothieno[3,2-c][1]benzothiepin-9-
      yl)propanamide 0.01 and tolterodine 3 mg/kg on bladder contraction in
      spinal cord injury rats was examined
      124937-52-6
IT
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
          (medicinal compns. containing tricyclic heterocyclic compound and
         anticholinergic agent)
RN
      124937-52-6 CAPLUS
CN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
      CRN
           124937-51-5
      CMF
           C22 H31 N O
Absolute stereochemistry. Rotation (+).
```

2 CM

87-69-4 CRN CMF C4 H6 O6

Absolute stereochemistry.

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 6 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 36 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

2005:57118 CAPLUS AN

DN 142:141276

TI Oxygen-containing heterocycles as PDE IV inhibitors, pharmaceutical compositions containing them and anticholinergic agents, uses of the compositions for treatment of COPD or asthma, and pharmaceutical kits containing both components

Abe, Yuzuru; Miki, Ichiro IN

MARPAT 142:141276

Kyowa Hakko Kogyo Co., Ltd., Japan PA

Jpn. Kokai Tokkyo Koho, 17 pp. SO

CODEN: JKXXAF

DT Patent

LA Japanese

FAN. CNT 1

05

IAN	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2005015394	A2	20050120	JP 2003-182385 JP 2003-182385	20030626 20030626

The compns. contain (a) O-containing benzoheterocycles I [m = 0-4; R1-R4 = H, AB lower alkyl, cycloalkyl, lower alkenyl, cycloalkenyl, aryl, aralkyl; 2 of R1-R4 on the same C are bonded together to form a spiro ring; adjacent 2 of R1-R4 may be bonded together to form a condensed ring or form a double bond; R5 = lower (halo)alkoxy; R6 = H, halo; Y = Q; R7 = cyano, ethynyl, carbamoyl; R8 = H, 4-carboxyphenyl; R7 andR8 may be bonded together to form a double bond] or their pharmacol. acceptable salts and (b) anticholinergic agents. COPD or asthma is treated by administering (a) and (b) simultaneously or sep. with some time interval. Thus, tablets were formulated containing cis-4-cyano-4-(8-methoxy-1,4-benzodioxan-5-yl)cyclobexanecarboxylic acid and oxybutynin bydrochloride.

yl)cyclohexanecarboxylic acid and oxybutynin hydrochloride.

Page 61

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

ANSWER 37 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11 2005:55181 CAPLUS ΑN 142:134324 DN TI Enantioselective synthesis of enantiomerically enriched compounds Piccolo, Oreste; Ulgheri, Fausta; Marchetti, Mauro IN PA Consiglio Nazionale Delle Ricerche, Italy **SO** PCT Int. Appl., 20 pp. CODEN: PIXXD2 DT Patent LA English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ____ PΙ wo 2005005356 Α2 20050120 WO 2004-EP7193 20040701 wo 2005005356 Α3 20050317 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
                 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
                 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
                 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
            RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
                 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
                 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
                 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
                 SN, TD, TG
                                                          IT 2003-MI1354
EP 2004-763070
                                                                                         20030702
      EP 1644311
                                  Α2
                                          20060412
                                                                                          20040701
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

IT 2003-MI1354 A 20030702
                                                          WO 2004-EP7193
                                                                                         20040701
os
      CASREACT 142:134324; MARPAT 142:134324
      A process for the enantioselective hydrogenation of formula I [W = CH2]
AB
      CO; X = OH, alkoxy, benzyloxy, etc.; Z = OH, alkoxy, benzyloxy with provisos] was disclosed. For example, compound II was enantioselectively reduced in the presence of [Rh(COD)Cl]2 and (S,S)-chiraphos to provide III
      in 84% and >99% e.e., which was subsequently converted to (S)-tolterodine. of note, this transformation is claimed in the presence of a catalyst or
      its suitable precursor based on Rh, Ru or Ir, having an oxidation state of 0, +1 or +2, and containing at least one enantiomerically enriched chiral ligand. 124937-52-6P
IT
      RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (USES)
           (enantioselective synthesis of enantiomerically enriched compds.)
RN
      124937-52-6 CAPLUS
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
       (2R, 3R) - 2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
             124937-51-5
      CRN
             C22 H31 N O
      CMF
```

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

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L11
        ANSWER 38 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
        2005:41309
AN
                          CAPLUS
        142:463446
DN
        Process for preparing N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-
TI
        phenylpropylamine in racemic or optically active form thereof
        Lustig, Petr; Hejtmankova, Ludmila; Ridvan, Ludek; Hruby, Petr; Kuchar,
IN
        Miroslav; Klouckova, Iveta; Sistek, Vaclav
PA
        Zentiva, A.S., Czech Rep.
        Czech Rep., 11 pp.
S<sub>0</sub>
        CODEN: CZXXED
DT
        Patent
        Czech
LA
FAN.CNT 1
        PATENT NO.
                                        KIND
                                                    DATE
                                                                       APPLICATION NO.
                                                                                                             DATE
                                         ____
                                                    20040714
                                                                       CZ 2003-1571
                                                                                                             20030605
PΙ
        CZ 293791
                                          в6
                                                                       CZ 2003-1571
                                                                                                             20030605
os
        CASREACT 142:463446
        The present invention relates to a process for preparing N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropylamine I (also known as tolterodine)
AB
       in racemic or optically active form thereof, comprising (a) 0-dealkylation and cyclization of the acid II [R1 = alkyl, CH2Ph], (b) reduction of the resulting 3,4-dihydro-6-methyl-4-phenyl-2H-benzopyran-2-one III, (c) reaction of IV with sulfonic acid derivative (e.g., p-toluenesulfonyl chloride), reacting V [X = toluenesulfonyl, methanesulfonyl, camphor-10-sulfonyl] with diisopropylamine, and hydrolysis of VI [X is defined as above] to afford I. Thus, reduction of rac-3,4-dihydro-6-methyl-4-phenyl-2H-benzopyran-2-one (rac-III) with Ped-All followed by reacting the
        phenyl-2H-benzopyran-2-one (rac-III) with Red-Al, followed by reacting the
        resulting rac-IV with p-toluenesulfonyl chloride, reacting rac-V [X =
        p-toluenesulfonyl] with diisopropylamine, and hydrolysis of rac-VI with
```

124937-52-6P RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparing N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropylamine in racemic or optically active form thereof)

RN 124937-52-6 CAPLUS
CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

IT

CRN 124937-51-5 CMF C22 H31 N O

NaOH afforded rac-I.

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 39 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2005:37484 CAPLUS

DN 142:309151

TI Effect of antacid on the pharmacokinetics of extended-release formulations of tolterodine and oxybutynin

AU Sathyan, Gayatri; Dmochowski, Roger R.; Appell, Rodney A.; Guo, Cindy; Gupta, Suneel K.

CS Department of Clinical Pharmacology, ALZA Corporation, Mountain View, CA, USA

SO Clinical Pharmacokinetics (2004), 43(14), 1059-1068 CODEN: CPKNDH; ISSN: 0312-5963

PB Adis International Ltd.

DT Journal LA English

In general, extended-release (ER) formulations are designed to prolong the duration of efficacy and reduce the adverse effects of a drug. These formulations often contain the entire daily dose in a single tablet. Therefore, failure of the ER mechanism not only diminishes the desired benefits, but may temporarily expose the patient to drug concns. higher than those released from a conventional tablet. In this study we determined whether pH has an effect on drug release from the ER formulations of oxybutynin (OROS technol.) and tolterodine (membrane coated beads) in vitro and in vivo. In vitro studies were based on standardized dissoln. expts. for each drug in media of different pH (artificial gastric fluid at pH 1.2, artificial intestinal fluid at pH 7.5, and water). In the two sep., identically designed in vivo studies, single doses of each drug were administered alone and with an antacid to male and female healthy volunteers aged 18-45 years. The randomized, crossover, open-label in vivo studies employed a validated assay to determine plasma concns. of tolterodine and its metabolite N-desethyloxybutynin. The in vitro study showed similar slow and steady drug release from ER-oxybutynin in each pH medium, with 64-71% released after 12 h. Drug release from ER-tolterodine

was steady and slow in artificial gastric fluid, with 72.5% of drug released after 12 h. However, drug release was much faster in artificial intestinal fluid and water, where 69.8% and 69.1%, resp., of the drug was released within 4 h. These in vitro results were consistent with the findings of the in vivo studies. In vivo, the pharmacokinetic profile (peak plasma concentration [Cmax] and area under the concentration-time curve)

of

ER-oxybutynin was similar after administration with or without antacid, whereas Cmax values of both tolterodine and 5-HM increased significantly when ER-tolterodine was administered with antacid (p \leq 0.017 vs ER-tolterodine alone). Changes in pH affected the release of tolterodine from ER-tolterodine, while they had no effect on the release of oxybutynin from the proprietary ER technol. used in ER-oxybutynin. The technol. employed in ER formulations thus dets. sensitivity of drug release to external factors.

IT

124937-52-6, Detrol RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug release from ER-tolterodine was faster in nonacidic medium in vitro while tolterodine and its metabolite 5-HM peak concns. increased with no effect on AUC, t1/2 when ER-tolterodine was co-administered with antacid in human)

RN CN

124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 40 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11 ΔN 2004:903965 CAPLUS 141:384269 DN Pharmaceutical compositions containing phosphodiesterase IV inhibitor and TI anticholinergic agents for treatment of respiratory diseases and their Abe, Yuzuru; Miki, Ichiro IN Kyowa Hakko Kogyo Co., Ltd., Japan PA Jpn. Kokai Tokkyo Koho, 19 pp. S0 CODEN: JKXXAF DT Patent Japanese LA FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE PΙ JP 2004300064 Α2 20041028 JP 2003-94507 20030331 JP 2003-94507 2003033 Tittle compns., useful for treatment of chronic obstructive pulmonary 20030331 AB disease and asthma, contain 7-[2-(3,5-dichloro-4-pyridyl)-1-oxoethyl]-4-methoxy-spiro(1,3-benzodioxole-2,1'-cyclopentane) (I) or its pharmacol. acceptable salts and anticholinergic agents. Thus, I tablets and oxybutynin hydrochloride tablets were formulated. 124937-52-6, Tolterodine tartrate IT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical compns. containing phosphodiesterase IV inhibitors and anticholinergic agents for treatment of respiratory diseases and their 124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME) RN CN CM

Absolute stereochemistry. Rotation (+).

124937-51-5

CMF C22 H31 N O

CM 2

CRN

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

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ANSWER 41 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
       2004:878262 CAPLUS
AN
       141:337803
DN
       Novel polymorphs of tolterodine tartrate
TI
      Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu;
Muralidhara, Reddy Dasari; Subash, Chander, Reddy Kesireddy
IN
      Hetero Drugs Limited, India
PA
       PCT Int. Appl., 14 pp.
SO
       CODEN: PIXXD2
DT
       Patent
LA
       English
FAN.CNT 1
                                  KIND
                                                            APPLICATION NO.
                                                                                            DATE
       PATENT NO.
                                            DATE
      WO 2004089281
                                   A2
                                            20041021
                                                            wo 2003-IN149
                                                                                            20030408
PΙ
      wo 2004089281
                                   Α3
                                            20041202
                 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
                 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
                 PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
                 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
            RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG 304037 A1 20041101 AU 2003-304037 20030408
      AU 2003304037
                                                                                            20030408
                                                            WO 2003-IN149
                                                            us 2003-510435
                                            20050616
                                                                                            20030408
      US 2005131067
                                   Α1
                                                            WO 2003-IN149
                                                                                        W 20030408
      The present invention relates to polymorphs of tolterodine tartrate, to
AΒ
       processes for their preparation and to pharmaceutical compns. containing them.
       process for preparation of tolterodine tartrate crystalline forms comprises the
       steps of (a) dissolving tolterodine free base in a suitable solvent; (b)
      adding tartaric acid; and (c) isolating tolterodine tartrate crystalline forms; wherein the suitable solvent is selected from ethanol, methylene
      dichloride, chloroform, acetone, acetonitrile, 1,4-dioxane, Et acetate, and Me tert-Bu ether, or (a) mixing tolterodine tartrate, an alc. and water, and (b) removing the solvents from the solution by freeze drying.
                                                                                                            For
      example, 2.0 g of tolterodine free base was dissolved in 25 mL of Et
      acetate and 1.2 g of tartaric acid was added to the solution. Then the contents were maintained for 2 h at 25° to 30° and filtered
       to give 2.2 g of tolterodine tartrate Form II.
IT
       124937-52-6P, Tolterodine tartrate
      RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP
      (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
           (preparation of crystalline forms of tolterodine tartrate for dosage forms)
       124937-52-6 CAPLUS
RN
       Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
       (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
```

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 С4 Н6 О6 CMF

Absolute stereochemistry.

ANSWER 42 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

2004:825265 CAPLUS AN

DN 142:336125

TI Process for preparing (R)-N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3phenylpropylamine (tolterodine)

Ridvan, Ludek; Hruby, Petr; Kuchar, Miroslav Zentiva, A.S., Czech Rep. Czech Rep., 7 pp. IN

PA

SO

CODEN: CZXXED

DT Patent

Czech LA

FAN. CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	cz 293509	 в6	20040512	cz 2003-531	20030221
				cz 2003-531	20030221

os CASREACT 142:336125; MARPAT 142:336125 The title compound I, useful for treating urinary incontinence (no data; no AB claimed activity), was prepared by optical resolution of racemic 3-(2-alkyloxy-5-methylphenyl)-3-phenylpropanoic acids and subsequent conversion of the corresponding (R)-(+)-acid II [R = alkyl, CH2Ph] to tolterodine. Thus, optical resolution of 3-(2-benzyloxy-5-methylphenyl)-3-phenylpropanoic acid (preparation given) followed by amidation of the (R)-(+)-acid with disopropylamine, reduction of the amide with synhydride, removal of the benzyl group, and treatment of the crude product with

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tartaric acid afforded I.tartrate.
     124937-52-6P, Tolterodine tartrate
IT
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP
        (process for preparing (R)-N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropylamine (tolterodine) starting from 3,4-dihydro-6-methyl-4-
         phenyl-2H-benzopyran-2-one)
     124937-52-6 CAPLUS
RN
     Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
     (2R, 3R) -2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
     CM
          124937-51-5
     CRN
     CMF C22 H31 N O
Absolute stereochemistry. Rotation (+).
         Ph
   OH
                    N(Pr-i)_2
  `Me
           2
     CM
     CRN
          87-69-4
     CMF C4 H6 06
Absolute stereochemistry.
          ÒН
     ANSWER 43 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
     2004:802289 CAPLUS
ΑN
DN
     141:301456
     New formulations for treatment of overactive bladder comprising
TI
     Nicklasson, Fredrik; Thyresson, Kristina; Lindberg, Nils-olof; Martino,
IN
     Alice C.; Lindell, Katarina
PΑ
     swed.
     U.S. Pat. Appl. Publ., 6 pp.
S0
     CODEN: USXXCO
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                                                APPLICATION NO.
                           KIND
                                   DATE
                                                                         DATE
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20040402
                                         20040930
                                                        us 2004-816673
PΙ
      US 2004191345
                                 Α1
                                                         SE 2003-830
                                                                                      20030326
                                                        US 2003-460214P
                                                                                      20030403
      AU 2004224556
                                 Α1
                                         20041007
                                                        AU 2004-224556
                                                                                      20040316
                                                         SE 2003-830
                                                                                      20030326
                                                        WO 2004-IB859
                                                                                      20040316
                                                        CA 2004-2519119
      CA 2519119
                                 AA
                                         20041007
                                                                                      20040316
                                                         SE 2003-830
                                                                                      20030326
                                                        WO 2004-IB859
                                                                                      20040316
      wo 2004084864
                                 A1
                                         20041007
                                                        WO 2004-IB859
                                                                                      20040316
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
                NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
                TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
           RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
                BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
                ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
                SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
                TD, TG
                                                        SE 2003-830
EP 2004-720944
                                                                                  A 20030326
      EP 1605920
                                 Α1
                                         20051221
                                                                                      20040316
               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK SE 2003-830 A 20030326
                                                        WO 2004-IB859
                                                                                      20040316
                                                                                  W
      BR 2004008743
                                                        BR 2004-8743
                                 Α
                                         20060328
                                                                                      20040316
                                                        SE 2003-830
                                                                                      20030326
                                                        WO 2004-IB859
                                                                                      20040316
                                                        CN 2004-80008087
                                         20060426
      CN 1764441
                                 Α
                                                                                      20040316
                                                        SE 2003-830
                                                                                      20030326
                                                        JP 2006-506376
      JP 2006521347
                                 T2
                                         20060921
                                                                                      20040316
                                                        SE 2003-830
                                                                                      20030326
                                                                                  Α
                                                        WO 2004-IB859
                                                                                  W
                                                                                      20040316
      A tolterodine-containing pharmaceutical formulation that comprises cocoa
AB
      powder, process for manufacturing the formulation and use of the formulation
for
      treating overactive bladder are described. For example, an oral composition
      was prepared containing tolterodine 1-tartrate 0.25%, hydrogenated soybean oil
      43.55%, cocoa powder 18.00%, mannitol 18.00%, maize starch 13.35%, Aspartame 0.15%, Acesulfame-K 0.10%, titanium dioxide 2.00%, monosodium glutamate 0.60%, mint and vanilla flavors 3.00%, and soy lecithin 1.00%. 124937-52-6, Tolterodine tartrate
IT
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
          (oral composition for treatment of overactive bladder comprising tolterodine
          and cocoa powder)
      124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
RN
CN
      (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
      CRN
            124937-51-5
            C22 H31 N O
      CMF
```

Absolute stereochemistry. Rotation (+).

Page 71

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

```
ANSWER 44 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2004:756674 CAPLUS
AN
      141:265984
DN
TI
      3,3-Diarylpropylamine derivatives and processes for isolation thereof
      Kumar, Yatendra; Prasad, Mohan; Kumar, Neela Praveen; Nayyar, Kaushal; Misra, Satyananda
ΙN
      Ranbaxy Laboratories Limited, India
PA
      PCT Int. Appl., 21 pp.
S0
      CODEN: PIXXD2
DT
      Patent
      English
LA
FAN.CNT 1
      PATENT NO.
                              KIND
                                       DATE
                                                      APPLICATION NO.
                                                                                  DATE
                                                      WO 2004-IB638
                                       20040916
                                                                                  20040308
PΙ
      wo 2004078700
                               Α1
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
          CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
               BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
               MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
               GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                                      IN 2003-DE237
                                                                                  20030306
                                                      AU 2004-218178
                                                                                   20040308
      AU 2004218178
                                Α1
                                       20040916
                                                      IN 2003-DE237
                                                                                  20030306
                                                      WO 2004-IB638
CA 2004-2517824
                                                                                  20040308
      CA 2517824
                                AA
                                       20040916
                                                                                   20040308
                                                      IN 2003-DE237
                                                                                  20030306
                                                      WO 2004-IB638
                                                                                  20040308
                                                                               W
                                       20051214
                                                      EP 2004-718361
                                                                                  20040308
      EP 1603862
                               Α1
               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK
```

IN 2003-DE237 A 20030306 WO 2004-IB638 W 20040308

The invention relates to 3,3-diarylpropylamines derivs. and processes for producing them. More particularly, it relates to the preparation of pure tolterodine or a pharmaceutically acceptable salt thereof and pharmaceutical compns. that include the pure tolterodine or a pharmaceutically acceptable salt thereof. It also relates to a novel 3,3-diarylpropylamine derivative, referred to as tolterodine dimer. Chemical, tolterodine dimer is N,N-di-[3-[2-hydroxy-5-methylphenyl]-3-phenylpropyl]isopropylamine.The invention also relates to use of pure tolterodine or tolterodine dimer as reference stds. or reference markers for checking the purity of tolterodine.

IT 124937-52-6P, Tolterodine tartrate

IT 124937-52-6P, Tolterodine tartrate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(3,3-diarylpropylamine derivs. and processes for isolation thereof)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 45 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:710573 CAPLUS

DN 141:355540

TI A validated chiral HPLC method for the enantiomeric separation of

tolterodine tartarate Kumar, Y. Ravindra; Ramulu, G.; Vevakanand, V. V.; Vaidyanathan, Gopal; Srinivas, Keesari; Kumar, M. Kishore; Mukkanti, K.; Reddy, M. ΑU Satyanarayana; Venkatraman, S.; Suryanarayana, M. V. Bulk Actives Unit-III, IDA-Bollaram, Dr. Reddy's Laboratories Ltd., CS Hyderabad, AP, 502325, India Journal of Pharmaceutical and Biomedical Analysis (2004), 35(5), 1279-1285 SO CODEN: JPBADA; ISSN: 0731-7085 Elsevier B.V. PB Journal DT LA English An isocratic chiral HPLC method was developed for the separation of tolterodine AB tartrate enantiomers. The mobile phase consists of n-hexane and iso-Pr alc. in the ratio of 980:20 (volume/volume) with 1 mL diethylamine and 0.6 mL trifluoroacetic acid. Chiralcel OD-H (250 mm + 4.6 mm) column was used at constant room temperature Flow rate was kept at 0.5 mL/min. is capable of detecting the S-isomer up to $0.1~\mu g/mL$. The method was validated in terms of linearity, precision, limit of detection (LOD), and limit of quantification (LOQ). 124937-52-6, Tolterodine tartrate
RL: ANT (Analyte); ANST (Analytical study)
(a_validated chiral HPLC method for the enantiomeric separation of IT tolterodine tartrate) 124937-52-6 CAPLUS RN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME) CM 124937-51-5 CRN C22 H31 N O CMF Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 С4 Н6 О6 CMF

RE.CNT 5

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ALL CITATIONS AVAILABLE IN THE RE FORMAT
L11
      ANSWER 46 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN
      2004:633513 CAPLUS
ΑN
       141:134132
DN
      Reduced dose of tolterodine and other antimuscarinic agents for treating
ΤI
      urinary disorders
      Korberly, Barbara H.; Danehower, Susan M.
IN
      Pharmacia AB, Swed.
PCT Int. Appl., 21 pp.
PA
S<sub>0</sub>
      CODEN: PIXXD2
DT
      Patent
      English
LΑ
FAN.CNT 1
      PATENT NO.
                                 KIND
                                          DATE
                                                          APPLICATION NO.
                                                                                         DATE
                                                          WO 2004-IB169
                                                                                         20040114
                                          20040805
PΙ
      wo 2004064821
                                  Α1
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
                 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI US 2003-441690P P 20030122
                                                          AU 2004-206110
      AU 2004206110
                                          20040805
                                  Α1
                                                                                         20040114
                                                          US 2003-441690P
                                                                                         20030122
                                                          WO 2004-IB169
                                                                                         20040114
                                                                                    W
      CA 2514022
                                          20040805
                                                          CA 2004-2514022
                                                                                         20040114
                                  AA
                                                          US 2003-441690P
                                                                                     Ρ
                                                                                         20030122
                                                          WO 2004-IB169
                                                                                    W
                                                                                        20040114
      EP 1589958
                                          20051102
                                                          EP 2004-702017
                                                                                         20040114
                                  Α1
                AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2003-441690P P 20030122
                                                          WO 2004-IB169
                                                                                         20040114
                                                          BR 2004-6861
                                                                                         20040114
      BR 2004006861
                                          20060103
                                                          US 2003-441690P
                                                                                         20030122
                                                          WO 2004-IB169
                                                                                        20040114
                                                                                    W
      CN 1741796
                                          20060301
                                                          CN 2004-80002565
                                                                                         20040114
                                                          US 2003-441690P
                                                                                         20030122
      JP 2006515607
                                          20060601
                                                          JP 2006-500313
                                  T2
                                                                                         20040114
                                                          US 2003-441690P ·
                                                                                    Ρ
                                                                                         20030122
                                                          wo 2004-IB169
US 2004-762726
US 2003-441690P
                                                                                    W
                                                                                         20040114
      US 2006047007
                                  Α1
                                          20060302
                                                                                         20040122
                                                                                        20030122
      The invention discloses a method, preferably an oral method, for treating urinary disorders, e.g. unstable or overactive bladder, while minimizing the occurrences of dry mouth, dyspepsia and reduced stream of tears. The
AB
     methods of the invention comprise orally administering to a mammal, preferably a human, a pharmaceutically ED of an antimuscarinic agent, such
      as tolterodine, when needed, whereby a symptomatic relief of urgency
      and/or frequency is achieved.
      124937-52-6, Detrol
IT
      RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
      activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
          (tolterodine or other antimuscarinic agent dose reduction for treatment of
          urinary disorders)
      124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
RN
CN
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
             1
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THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 47 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2004:428812 CAPLUS
ΑN
      140:412343
DN
      Combination therapy for postmenopausal female sexual dysfunction
TI
      comprising an androgen, an estrogen and an antimuscarinic
      Bilkey, Chris R.; Slatter, Greg J.
IN
PA
      Pharmacia & Upjohn Company, USA
SO
      PCT Int. Appl., 27 pp.
      CODEN: PIXXD2
DT
      Patent
LA
      English
FAN.CNT 1
      PATENT NO.
                                KIND
                                                         APPLICATION NO.
                                                                                        DATE
                                          DATE
PI
      wo 2004043429
                                 A1
                                          20040527
                                                         wo 2003-us34418
                                                                                        20031029
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
                CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
                GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
                LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
               OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
                BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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US 2002-425537P P 20021112 AU 2003287248 A1 20040603 AU 2003-287248 20031029 US 2002-425537P P 20021112 WO 2003-US34418 W 20031029

As set of pharmaceutical dosage forms is provided, each comprising an androgen and at least one agent selected from the group consisting of an estrogen and an antimuscarinic, in total and relative dosage amts. that are therapeutically effective in treatment of female sexual dysfunction (FSD) or postmenopausal sexual avoidance (PMSA), said dosage forms being adapted for intravaginal administration. A method of treatment of FSD or PMSA comprises administering intravaginally, in a treatment regimen extending over a period of at least 7 days, dosage forms at least a portion of which comprise an androgen and at least one agent selected from the group consisting of an estrogen and an antimuscarinic, in total and relative dosage amts. that are therapeutically effective in treatment of FSD or PMSA, wherein no more than one dosage form is administered on any day. Also provided is a kit useful in implementing such a treatment regimen.

IT 124937-52-6, Tolterodine tartrate
 RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(combination therapy for postmenopausal female sexual dysfunction comprising an androgen, an estrogen and an antimuscarinic)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 9 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 48 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

2004:410936 CAPLUS AΝ

141:46646 DN

Management of overactive bladder: defining the role of extended-release TI tolterodine

Keam, Susan J.; Perry, Caroline M. ΑU

- Adis International Inc., Yardley, PA, USA
 Disease Management & Health Outcomes (2004), 12(2), 121-142 SO CODEN: DMHOFV; ISSN: 1173-8790 Adis International Ltd.
- PΒ
- Journal; General Review DT

English ΙΑ

AB

A review. Overactive bladder (OAB), a common condition affecting pprox 16-17% of adult men and women in Europe and the US, is characterized by symptoms of urinary urgency, with or without urge urinary incontinence (UUI), usually with micturition frequency and nocturia. OAB is thought to result from abnormal, involuntary detrusor contractions during bladder filling. The symptoms of OAB have a considerable adverse effect on quality of life (QOL) in affected patients, and are associated with an increased risk of comorbidities, and increased direct and indirect costs. Management of OAB focuses on symptom improvement, and includes nonpharmacol. and pharmacol. therapy. Extended-release tolterodine (Detrusitol XL, Detrol LA, Detrusitol SR, Detrusitol Neo, Detrusitol Retard, Unidet LA) is an oral, once-daily, nonselective, competitive antimuscarinic drug. It acts on smooth muscle motor efferent pathways, including bladder detrusor muscle, and is a first-line therapy for OAB. Extended-release tolterodine is at least as effective as immediate-release tolterodine in improving UUI and other symptoms associated with OAB (including urinary frequency, urge symptoms, voided volume/micturition), and in improving health-related QOL. It has similar efficacy to oral immediate- or extended-release oxybutynin, or transdermal oxybutynin. The likelihood of dry mouth, the most bothersome anticholinergic adverse effect associated with antimuscarinic drugs, is significantly reduced with extended-release tolterodine in patients with OAB compared with immediate-release tolterodine. Dry mouth also occurs significantly less frequently with extended-release tolterodine than with immediate- or extended-release oxybutynin. The incidence of dry mouth with extended-release tolterodine or transdermal oxybutynin is similar. economic models, extended-release tolterodine is more cost effective in patients with OAB than no treatment, or treatment with immediate-release tolterodine or immediate-release oxybutynin, and is as cost effective as extended-release oxybutynin. In conclusion, clin. and economic data support the use of extended-release tolterodine as a first-line therapy in the management of adult patients with OAB. It is at least as effective as immediate-release tolterodine, but is associated with a lower incidence of dry mouth. Moreover, the convenient once-daily administration regimen dry mouth. Moreover, the convenient once-daily administration regimen offers the potential for good compliance. The favorable efficacy and tolerability profile of extended-release tolterodine has been demonstrated for up to 12 mo. Extended-release tolterodine is as effective as oral immediate- or extended-release oxybutynin, but is better tolerated in terms of dry mouth. It has similar efficacy and tolerability (including dry mouth) to transdermal oxybutynin. Extended-release tolterodine is, therefore, a valuable first-line therapy in the treatment of OAB. 124937-52-6, Detrusitol

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (extended-release tolterodine in management of overactive bladder)

RN 124937-52-6 CAPLUS

IT

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 144 THERE ARE 144 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
ANSWER 49 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
         2004:203653 CAPLUS
ΑN
         140:241060
DN
         Oral liquid tolterodine compositions
TI
         Reo, Joseph P.; Kienle, Kathryn M.; Fredrickson, Jennifer K.
IN
PA
         Pharmacia Corporation, USA
         PCT Int. Appl., 29 pp.
50
         CODEN: PIXXD2
DT
         Patent
LA
         English
FAN.CNT 1
         PATENT NO.
                                            KIND
                                                        DATE
                                                                             APPLICATION NO.
                                                                                                                      DATE
                                            ____
                                                        20040311
                                                                            wo 2003-US26675
                                                                                                                      20030825
PI
        wo 2004019925
                                             Α1
                      AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

W: AE, AG, AL, AM, AI, AU, AZ, BA, BB, BG, BK, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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AB

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KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-406429P P 20020828
                                      20040311
                                                    CA 2003-2496806
                                                                               20030825
     CA 2496806
                              AA
                                                    US 2002-406429P
                                                                               20020828
                                                    wo 2003-us26675
                                                                               20030825
                                                    AU 2003-265680
                                                                               20030825
     AU 2003265680
                              Α1
                                     20040319
                                                    US 2002-406429P
                                                                               20020828
                                                    wo 2003-US26675
                                                                           W
                                                                               20030825
     us 2005032905
                              Α1
                                      20050210
                                                    us 2003-647816
                                                                               20030825
      us 7101888
                              B2
                                      20060905
                                                    US 2002-406429P
                                                                               20020828
                                                    EP 2003-791779
                                     20050608
     EP 1536780
                              Α1
                                                                               20030825
               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
          R:
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                                    US 2002-406429P
                                                                               20020828
                                                    wo 2003-US26675
                                                                               20030825
     BR 2003013714
                                     20050628
                                                    BR 2003-13714
                                                                               20030825
                                                    US 2002-406429P
                                                                               20020828
                                                   wo 2003-US26675
                                                                               20030825
                                                    JP 2004-531469
     JP 2006500381
                              T2
                                      20060105
                                                                               20030825
                                                    US 2002-406429P
                                                                            Ρ
                                                                               20020828
     WO 2003-US26675 W 20030825
A pharmaceutical composition in a form of an oral liquid comprises water having
     in solution therein a water-soluble salt of a tolterodine-related compound at a
     concentration in the composition The composition has a pH of about 2-6 and
further
      comprises a sweetening agent and an antimicrobial agent at a concentration that
      is antimicrobially effective at the pH of the composition The composition is
useful
     for treating a muscarinic receptor-mediated disorder, more particularly
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overactive bladder, in a subject by orally administering to the subject an effective amount of the composition Thus, a formulation contained tolterodine L-tartrate 0.2, 85% sucrose solution 382.42, 70% sorbitol solution 54, citric acid 5.88, sodium citrate 5, sodium benzoate 1, artificial wild cherry flavor 1, and SweetAm powder 0.5 mg, and water qs to 1 mL. 124937-52-6, Tolterodine tartrate

IT

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oral liquid tolterodine compns.)

RN 124937-52-6 CAPLUS

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

124937-51-5 C22 H31 N O CMF

Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 CMF C4 H6 06

Absolute stereochemistry.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 50 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

2003:1007337 CAPLUS AN

140:53286 DN

Clinical efficacy and tolerability of extended-release tolterodine and ΤI immediate-release oxybutynin in Japanese and Korean patients with an overactive bladder: a randomized, placebo-controlled trial Homma, Y.; Paick, J. S.; Lee, J. G.; Kawabe, K. Japanese and Korean Tolterodine Study Group, Department of Urology, Tokyo

ΑU

CS

University, Tokyo, Japan BJU International (2003), 92(7), 741-747 CODEN: BJINFO; ISSN: 1464-4096 S0

Blackwell Publishing Ltd. PB

Journal DT

LA English

AB

Objective: To compare extended-release (ER) tolterodine and immediate-release (IR) oxybutynin with placebo in Japanese and Korean patients with an overactive bladder (OAB). Patients and Methods: Men and women aged ≥ 20 yr with symptoms of urinary urgency, urinary frequency (\geq 8 micturitions/24 h), urge incontinence (\geq 5 episodes/wk) and symptoms of OAB for \geq 6 mo were randomized to double-blind treatment with tolterodine ER 4 mg once daily, oxybutynin IR 3 mg three times daily or placebo for 12 wk. Efficacy assessments included changes from baseline in nos. of incontinence episodes per wk, voids/24 h and mean volume voided/void. Patient perceptions of bladder condition, urgency and treatment benefit were also assessed. Results: In all, 608 patients were randomized to treatment with tolterodine (240), oxybutynin (246) or placebo (122). More patients prematurely withdrew on oxybutynin (23%) than with tolterodine (10.4%) or placebo (16.4%). After 12 wk of treatment, the median number of incontinence episodes/wk was reduced significantly more in the tolterodine (79%; P = 0.0027) and oxybutynin groups (76.5%; P = 0.0168) than on placebo (46.4%). There were also significantly greater improvements in the number of voids/24 h and volume voided/void with tolterodine and oxybutynin than with placebo. More patients in the tolterodine and oxybutynin than in the placebo groups reported improvements in perceived bladder condition, ability to hold urine and treatment benefit. Patients treated with oxybutynin reported more adverse events than those treated with tolterodine or placebo. Dry mouth was significantly more common with oxybutynin than with tolterodine (53.7% vs. 33.5%; P < 0.001), and occurred in 9.8% of placebo patients. Conclusion: Tolterodine ER has similar efficacy but is better tolerated than oxybutynin IR in Japanese and Korean patients with OAB. 124937-52-6, Detrol

IT

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (extended-release tolterodine vs. immediate-release oxybutynin in Japanese and Korean patients with overactive bladder)

124937-52-6 CAPLUS RN

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 C22 H31 N O CMF

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 С4 Н6 О6 CMF

Absolute stereochemistry.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 51 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN AN 2003:971836 CAPLUS

140:23256 DN

TI Combination therapy for treatment of amyotrophic lateral sclerosis (ALS) with cyclooxygenase-2 (COX 2) inhibitor(s) and a second drug

IN Isakson, Peter C.

PA Pharmacia Corporation, USA

SO PCT Int. Appl., 358 pp.

CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 1

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                                                       wo 2003-US14547
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os
      MARPAT 140:23256
AB
      A method of treating, preventing, or inhibiting ALS, in a subject in need
      of such treatment, inhibition or prevention. The method comprises
      administering to a subject one or more cyclooxygenase-2 selective
      inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s),
      ester(s), or prodrug(s) thereof, in combination with one or more second drugs, wherein the amount of the cyclooxygenase-2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof in combination with the amount of second drug(s) constitutes an ALS
      treatment, inhibition or prevention effective amount 124937-52-6, Detrol
IT
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses)
          (combination therapy for amyotrophic lateral sclerosis treatment of
          with COX-2 inhibitor and second drug)
      124937-52-6
                     CAPLUS
RN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
            124937-51-5
      CRN
      CMF
            C22 H31 N O
Absolute stereochemistry. Rotation (+).
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CM 2

CRN 87-69-4 CMF C4 H6 O6

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ANSWER 52 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN /
L11
      2003:836606 CAPLUS
AN
      139:328349
DN
     Tolterodine and hydroxytolterodine salts and their use as pharmaceuticals
TI
      Hawley, Michael; Singh, Satish Kumar; Morozowich, Walter; Warchol, Mark P.
IN
PA
      Pharmacia & Upjohn Company, USA
     U.S. Pat. Appl. Publ., 9 pp.
SO
     CODEN: USXXCO
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OS MARPAT 139:328349

The present invention concerns novel pharmaceutically active compds., pharmaceutical compns. containing the same, the compds. for use as medicaments, and use of the compds. for the manufacture of specific medicaments. The present invention also concerns a method of treatment involving administration of the compds. by inhalation and insufflation. Specifically, the compds. are pharmaceutically acceptable salts of tolterodine or hydroxytolterodine, wherein the salt is of an acid selected from the group consisting of aliphatic mono- and dicarboxylic acids comprising from 7 to 24 carbon atoms, alkanedisulfonic acids comprising from 2 to 4 carbon atoms, naphthoic acid derivs. comprising from 11 to 27 carbon atoms, maleic acid and fumaric acid.

IT 124937-52-6, Tolterodine tartrate

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tolterodine and hydroxytolterodine salts for inhalation)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absoluțe stereochemistry. Rotation (+).

CM 2

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CRN 87-69-4
CMF C4 H6 06
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Absolute stereochemistry.

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RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
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      139:281288
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U.S., 7 pp., Cont.-in-part of Appl. No. PCT/SE99/02052.
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	20000 7624		66		A5 B2	2000 2003	0529 0626	AU	1998- 1999- 1999- 2000-	14300	,		1999	TIII
BR	9915:	142	٠		Α	2001	.0807	WO WO BR	1998- 1999- 1999-	SE146 SE205 15142	2	W	1999	1111 1111
ЕP	11288	819			A1	2001	.0905	WO WO	1998- 1999- 1999-	SE146 SE205	2	Α	1999	0826
EP	11288 R:	AT,	ΒE,	CH,	DE,	2001 2003 DK, ES, FI, RO		GB, G		LI,		NL, S	1000	
EE	2001	00254	4		Α	2002	1216	WO WO EE SE	1999- 1999- 2001- 1998-	SE146 SE205 254 3871	2	W W A	1999 1999 1999 1998	0826 1111 1111 1111
	2003: 36160		46		T2 B2	2003 2005	0527 0202	J.P.	1999- 1999- 2000-	SE205 58059	52 5	A W	1999 1999	1111 1111
NZ	5114	30			A	2003	0530	WO WO NZ	1998- 1999- 1999-	SE205 51143	2	A A W	1999	1111 1111
ΑT	2474!	58			E	2003	0915	WO WO	1998- 1999- 1999-	SE146 SE205	2	A W W		0826 1111
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	2847!				В6			SE WO WO	1998- 1999- 1999-	3871 SE146 SE205	2	A A A	1998 1999 1999	1111 0826 1111
TW	22287	79			В1	2004	1101	TW	2000-	89102	338		2000	0211

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W: AE, AL, CZ, DE, IN, IS, MD, MG, SK, SL,	AL AM, AT, DK, DM, JP, KE, MK, MN, TJ, TM, KE, IS.	AU, AZ, BA, EE, ES, FI, KG, KP, KR, MW, MX, NO, TR, TT, TZ, MW, MZ, SD.	WO 2000-SE2061 BB, BG, BR, BY, CA, GB, GD, GE, GH, GM, KZ, LC, LK, LR, LS, NZ, PL, PT, RO, RU, UA, UG, US, UZ, VN, SL, SZ, TZ, UG, ZW, IE, IT, LU, MC, NL, ML, MR, NE, SN, TD,	20001024 CH, CN, CR, CU, HR, HU, ID, IL, LT, LU, LV, MA, SD, SE, SG, SI, YU, ZA, ZW AT, BE, CH, CY, PT, SE, BF, BJ, TG
AU 2001013192	A5 B2	20010606 20060202	WO 1999-SE2052 SE 2000-782 AU 2001-13192	A 19991111 A 20000309 20001024
		20020625	WO 1999-SE2052 SE 2000-782 WO 2000-SE2061 BR 2000-15346 WO 1999-SE2052 SE 2000-782 WO 2000-SE2061	w 20001024
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ни 200203028	A2	20030228	SE 2000-782 WO 2000-SE2061 HU 2002-3028	W 19991111 A 20000309 W 20001024 20001024 W 19991111 A 20000309
JP 2003513918	т2	20030415	WO 2000-SE2061 JP 2001-536139 WO 1999-SE2052 SE 2000-782	W 20001024 20001024 A 19991111
NZ 518309	Α	20030530	WO 2000-SE2061 NZ 2000-518309 WO 1999-SE2052	W 20001024 20001024 A 19991111
EE 200200245	Α	20030616	SE 2000-782 WO 2000-SE2061 EE 2002-245 WO 1999-SE2052 SE 2000-782	A 20000309 W 20001024 20001024 A 19991111 A 20000309
AT 300941	E	20050815	WO 2000-5E2061 AT 2000-975092 WO 1999-5E2052 SE 2000-782	A 20000309 W 20001024 20001024 A 19991111 A 20000309
PT 1227806	т	20051031	WO 2000-SE2061 PT 2000-975092 WO 1999-SE2052	W 20001024 20001024 W 19991111
ES 2245320	Т3	20060101	SE 2000-782 ES 2000-975092 WO 1999-SE2052 SE 2000-782	A 20000309 20001024 A 19991111 A 20000309
us 6630162	B1	20031007	US 2000-708428 WO 1999-SE2052 SE 2000-782	A2 19991111 A 20000309

	ZA 2003	1003575	Α	20020503	US 2000-202862P ZA 2001-3575 SE 1998-3871	P 20000510 20010503 A 19981111
	NO 2001	L002314	Α	20010709	NO 2001-2314 SE 1998-3871 WO 1999-SE1463	20010510 A 19981111 W 19990826
	HR 2000	L000333 L0333	A1 B1	20030430 20041031	WO 1999-SE2052 HR 2001-333	w 19991111 20010510
	BG 1055		A	20011231	SE 1998-3871 WO 1999-SE1463 WO 1999-SE2052 BG 2001-105582	A 19981111 A 19990826 W 19991111 20010608
				,	SE 1998-3871 WO 1999-SE1463 WO 1999-SE2052	A 19981111 W 19990826 W 19991111
	нк 1040	917	A1	20050527	HK 2002-102521 SE 1998-3871 WO 1999-SE1463 WO 1999-SE2052	20020404 A 19981111 A 19990826 A 19991111
	ZA 2002	2002767	Α .	20030409		20020409 A 19991111
	NO 2002	2002264	Α	20020513	NO 2002-2264	20020513 W 19991111 A 20000309 W 20001024
FAN	2001:35 PATENT		KIND	DATE	APPLICATION NO.	DATE
PI	W:	AE, AL, CZ, DE, IN, IS, MD, MG, SK, SL, GH, GM, DE, DK,	DK, DM, JP, KE, MK, MN, TJ, TM, KE, LS, ES, FI,	AU, AZ, BA, EE, ES, FI, KG, KP, KR, MW, MX, NO, TR, TT, TZ, MW, MZ, SD, FR, GB, GR,	BB, BG, BR, BY, CA, GB, GD, GE, GH, GM, KZ, LC, LK, LR, LS, NZ, PL, PT, RO, RU, UA, UG, US, UZ, VN, SL, SZ, TZ, UG, ZW, IE, IT, LU, MC, NL,	HR, HU, ID, IL, LT, LU, LV, MA, SD, SE, SG, SI, YU, ZA, ZW AT, BE, CH, CY, PT, SE, BF, BJ,
	1.0 200	CF, CG,	CI, CM,	GA, GN, GW,	ML, MR, NE, SN, TD, WO 1999-SE2052 SE 2000-782	A 19991111 A 20000309
	WO 2000 W:	AE, AL, CZ, DE, IN, IS, MD, MG, SK, SL, GH, GM, DK, ES,	DK, DM, JP, KE, MK, MN, TJ, TM, KE, LS, FI, FR,	EE, ES, FI, KG, KP, KR, MW, MX, NO, TR, TT, TZ, MW, SD, SL, GB, GR, IE,	BB, BG, BR, BY, CA, GB, GD, GE, GH, GM, KZ, LC, LK, LR, LS, NZ, PL, PT, RO, RU, UA, UG, US, UZ, VN, SZ, TZ, UG, ZW, AT, IT, LU, MC, NL, PT,	CH, CN, CR, CU, HR, HU, ID, IL, LT, LU, LV, MA, SD, SE, SG, SI, YU, ZA, ZW BE, CH, CY, DE,
	CA 2387		CM, GA,	GN, GW, ML, 20010517	MR, NE, SN, TD, TG SE 1998-3871 WO 1999-SE1463 CA 2000-2387973	A 19981111 W 19990826 20001024
	•		,		WO 1999-SE2052 SE 2000-782 WO 2000-SE2061	A 19991111 A 20000309 W 20001024
	AU 2001 AU 7841		A5 B2	20010606 20060202	AU 2001-13192 WO 1999-SE2052	20001024 A 19991111
					SE 2000-782	A 20000309

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                                             SE 2000-782
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                                             WO 2000-SE2061
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EP 1227806
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EP 1227806
                        В1
                               20050803
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     R:
         IE, SI, LT, LV, FI, RO, MK, CY, AL
                                             WO 1999-SE2052
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                                             SE 2000-782
                                                                        20000309
                                             WO 2000-SE2061
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                        Α2
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ни 200203028
                                             HU 2002-3028
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                                             WO
                                             SE 2000-782
                                                                        20000309
                                                                     Α
                                             WO 2000-SE2061
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JP 2003513918
                        T2
                               20030415
                                             JP 2001-536139
                                                                        20001024
                                             WO 1999-SE2052
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                                                                        19991111
                                             SE 2000-782
                                                                        20000309
                                             WO 2000-SE2061
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                               20030530
                                             NZ 2000-518309
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NZ 518309
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                                             WO 1999-SE2052
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                                                                        20000309
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                                             WO
                                                 2000-SE2061
                                                                        20001024
EE 200200245
                                                 2002-245
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                               20030616
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                                             SE 2000-782
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AT 300941
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                               20050815
                                             AT 2000-975092
                                                                        20001024
                                             WO 1999-SE2052
                                                                        19991111
                                             SE 2000-782
                                                                        20000309
                                             WO 2000-SE2061
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NO 2002002264
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                                             WO 1999-SE2052
                                                                        19991111
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                                             SE 2000-782
                                                                    Α
                                                                        20000309
                                             WO 2000-SE2061
                                                                    W
                                                                        20001024
The invention relates to a pharmaceutical formulation containing tolterodine,
a tolterodine-related compound, or a pharmacol. acceptable salt thereof, as
active ingredient. The formulation exhibits a controlled in vitro release
of the active ingredient in phosphate buffer at pH 6.8 of not less than
about 80% after 18 h. After oral administration to a patient the
formulation is capable of maintaining a substantially constant serum level
of the active moiety or moieties for 24 h. The invention also relates to the use of the pharmaceutical formulation for treating overactive bladder
and gastrointestinal disorders. For example, controlled-release beads with a three-layer coating were prepared Starch-containing sugar spheres (cores) were coated with a Surelease seal coat, a tolterodine tartrate/hydroxypropyl Me cellulose (HPMC) layer, and a Surelease/HPMC
final layer. After tray drying, the coated spheres were filled into hard
gelatin capsules to obtain 2 mg and 4 mg tolterodine L-tartrate capsules.
124937-52-6, Tolterodine tartrate
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (controlled-release oral formulations for tolterodine)
124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
CM
     1
     124937-51-5
CRN
     C22 H31 N O
CMF
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AB

IT

RN

CN

Page 93

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 54 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN 2003:678653 CAPLUS
L11
ΑN
      139:207821
DN
      Use of cyclooxygenase inhibitors and antimuscarinic agents for the
TI
      treatment of incontinence
IN
      Versi, Ebrahim
      Pharmacia Corporation, USA
PA
SO
      PCT Int. Appl., 51 pp.
      CODEN: PIXXD2
DT
      Patent
LA
      English
FAN.CNT 1
      PATENT NO.
                              KIND
                                      DATE
                                                     APPLICATION NO.
                                                                                 DATE
                                      20030828
                                                                                 20030214
      wo 2003070233
                               Α1
                                                     wo 2003-US4561
PΙ
               AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
               CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
               GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
               LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
               PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
               UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
               KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002-357888P

P 20020219
                                                     CA 2003-2475374
     CA 2475374
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                                                     us 2002-357888P
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wo 2003-US4561

20030214

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A1
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                                                          AU 2003-211078
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      AU 2003211078
                                                          US 2002-357888P
                                                                                         20020219
                                                          wo 2003-US4561
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                                                                                         20030214
      EP 1476146
                                  Α1
                                                          EP 2003-742765
                AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                                          US 2002-357888P
                                                                                         20020219
                                                          wo 2003-US4561
                                                                                         20030214
                                                          BR 2003-7772
US 2002-357888P
      BR 2003007772
                                          20041207
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                                                          wo 2003-US4561
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                                                          CN 2003-804160
                                                                                         20030214
      CN 1633283
                                          20050629
                                  Α
                                                          US 2002-357888P
                                                                                         20020219
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      JP 2005526040
                                  T2
                                          20050902
                                                          US 2002-357888P
                                                                                         20020219
                                                          wo 2003-US4561
                                                                                         20030214
                                          20031009
                                                          US 2003-368091
      US 2003191172
                                  A1
                                                                                         20030218
                                                          US 2002-357888P
                                                                                         20020219
      The invention provides a method for the use of a cyclooxygenase-2
AB
      inhibitor, alone or in combination with an antimuscarinic agent, for the treatment or prophylaxis of a urinary incontinence condition in a subject in need of such treatment or prevention, comprising administering to the subject an effective amount of the cyclooxygenase-2 inhibitor and, optionally, the antimuscarinic agent.

124937-52-6, Tolterodine tartrate
IT
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
      (Biological study); USES (Uses) (cyclooxygenase inhibitors and antimuscarinic agents for treatment of
          incontinence)
      124937-52-6 CAPLUS
RN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
      CRN
            124937-51-5
            C22 H31 N O
      CMF
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Absolute stereochemistry. Rotation (+).

CRN 87-69-4 CMF C4 H6 O6

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 10 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 55 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN 2003:652747 CAPLUS L11

AN

140:31465 DN

Sustained-release preparation of tolterodine tartrate and preparing TI thereof

IN Cao, Deshan; Liu, Zhenghe

PA Meirui Pharmaceutical Co., Ltd., Peop. Rep. China Faming Zhuanli Shenqing Gongkai Shuomingshu, 10 pp. S0 CODEN: CNXXEV

DT Patent Chinese LA

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE 20021009 20020109 PΙ Α CN 2002-112512 CN 1372923 CN 2002-112512 20020109

Tolterodine tartrate sustained-release prepns. (such as granules, tablets, AB pills, or capsules) for treating bladder diseases is composed of tolterodine tartrate 1, C3-20 aliphatic carboxylic acid (such as tartaric acid, malic acid, succinic acid, glutaric acid, glutamic acid, maleic acid, mandelic acid, and/or citric acid) and/or alditol (such as mannitol, xylitol, lactose, or sucrose) 2-50, cellulose or its derivative (such as microcryst. cellulose, hydroxypropyl cellulose, hydroxypropyl Me cellulose, and/or Na CM-cellulose) 1-100, dextrin 2-50, polyvinylpyrrolidone 1-50, and lubricant (such as talc, stearic acid, or Mg stearate) 0.1-5 part.

124937-52-6, Tolterodine tartrate IT

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sustained-release preparation of tolterodine tartrate)

124937-52-6 CAPLUS RN

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-. CN (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

1 CM

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

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CM 2
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CRN 87-69-4 CMF C4 H6 O6

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ANSWER 56 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
       2003:511139 CAPLUS
AN
       139:74052
DN
       Controlled release dosage forms containing polymers
ΤI
       Aldrich, Dale S.; Wald, Randy J.; Hlinak, Anthony J.; Bandyopadhyay, Rebanta; Coffey, Martin J.; Goll, Diane; Mazhary, Ahmad M.; Meury, Richard H.; Rohrs, Brian R.; Skoug, John W.; Secreast, Stephen L.; Stelzer, Dennis J.; White, Jackie G. Pharmacia Corporation, USA; et al.
IN
PA
       PCT Int. Appl., 30 pp.
SO
       CODEN: PIXXD2
DT
       Patent
       English
LA
FAN.CNT 1
                                                                   APPLICATION NO.
                                                                                                       DATE
                                      KIND
                                                 DATE
       PATENT NO.
                                                 20030703
                                                                   wo 2002-US41037
                                                                                                       20021219
PΙ
       wo 2003053428
                                       Α1
                   AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
                    PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
                    UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
              RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                    KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
                   FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
                   CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2001-342650P P
                                                                                                  P 20011220
                                                                   AU 2002-360717
US 2001-342650P
       AU 2002360717
                                                 20030709
                                                                                                       20021219
                                        A1
                                                                                                       20011220
                                                                                                  Ρ
                                                                   wo 2002-US41037
                                                                                                       20021219
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                                                                   US 2002-325298
                                                                                                       20021219
       US 2003152624
                                        Α1
                                                 20030814
                                                                   US 2001-342650P
                                                                                                  Ρ
                                                                                                       20011220
       Controlled release pharmaceutical compns. comprising tolterodine and a
AB
       polymer-based release-controlling component and processes for preparing such
       compns. are provided. The compns. are useful in the treatment of
       overactive bladder and similar conditions. Thus, a coated bead formulation comprised in the core sugar spheres 73.3%; the first layer contained Surelease E-7-19010 Clear 11.9, and water qs; the second layer comprised tolterodine L-tartrate 2.2, HPMC-2910 1.7%, and water qs; the third layer was composed of Surelease 7-19010 8.5, HPMC-2910 1.4% and
       water qs; the 4th layer HPMC-2910 1.0%, and water qs (water removed during
       processing).
       124937-52-6
IT
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (controlled release dosage forms containing polymers)

RN 124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5
CMF C22 H31 N 0

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 57 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
        2003:511071 CAPLUS
139:47218
ΑN
DN
       Vaginal delivery of drugs for the treatment of urogenital diseases
Dipiano, Gerianne Tringali; Ziemniak, John A.; Janicki, Thomas I.
TI
IN
        Femmepharma, Inc., USA
PCT Int. Appl., 33 pp.
PA
SO
        CODEN: PIXXD2
DT
        Patent
LA
        English
FAN.CNT 1
        PATENT NO.
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                                                                      APPLICATION NO.
                                                   DATE
                                                                                                           DATE
ΡI
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       wo 2003053292
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                UG, UZ, VN, YU, ZA, ZM, ZW
           RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
                FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
                CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                                                                                   20021219
                                A1
                                                      US 2001-342663P
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      EP 1455697
                                       20040915
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      Drug delivery compns. which are suitable for vaginal administration for
the treatment of diseases and disorders in the urogenital tract are
AB
                    The compns. may be in the form of a tablet, liquid suspension or
      described.
      dispersion, dried powder, topical ointment, cream, foam, suppository, or aerosol. The drug delivery compns. are administered directly to the vagina and do not require the use of a solid device. This method of
      administration reduces the systemic levels of the drugs.
      124937-52-6, Tolterodine tartrate
IT
      RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vaginal delivery of drugs for treatment of urogenital diseases)
      124937-52-6 CAPLUS
RN
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CN
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      CMF
Absolute stereochemistry.
                                 Rotation (+).
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OH Ph R N(Pr-i)2

CM 2

CRN 87-69-4

Me

CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 58 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN
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AN
     138:406917
DN
     Buccal sprays or capsules containing drugs for treating disorders of the
TI
     gastrointestinal or urinary tracts
IN
     Dugger, Harry A., III
PA
     USA
     U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 537,118.
SO
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US 2000-537118 A2 20000329 US 2002-230073 A2 20020829 US 2003-671708 A3 20030929

AB Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation I: aqueous polar solvent, active compound, and optional flavoring agent; formulation II: aqueous polar solvent, active compound, optionally flavoring agent, and propellant; formulation III: non-polar solvent, active compound, and optional flavoring agent; and formulation IV: non-polar solvent, active compound, optional flavoring agent, and propellant. A lingual spray contained famotidine 7-20, water 5-10, L-aspartic acid 5-10, polyethylene glycol 50-85, and flavors 2-5%.

IT 124937-52-6, Detrol

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal sprays or capsules containing drugs for treating disorders of
gastrointestinal or urinary tracts)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 59 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN

AN 2003:376645 CAPLUS

DN 138:374201

TI Compositions for treatment of postmenopausal female sexual dysfunction

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Bilkey, Chris R.; Slatter, Greg J.; Versi, Ebrahim
IN
      Pharmacia Corporation, USA
PA
      PCT Int. Appl., 26 pp.
50
      CODEN: PIXXD2
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A set of pharmaceutical dosage forms is provided, each comprising at least two therapeutic agents selected from (a) an estrogen, (b) an androgen, and (c) an antimuscarinic, in total and relative dosage amts. that are therapeutically effective in treatment of female sexual dysfunction (FSD) or postmenopausal sexual avoidance (PMSA), the dosage forms being adapted for intravaginal administration. A method of treatment of FSD or PMSA comprises administering intravaginally, in a treatment regimen extending over a period of at least 7 days, dosage forms at least a portion of which comprise two or more therapeutic agents selected from (a) an estrogen, (b) an androgen, and (c) an antimuscarinic, in total and relative dosage amts. that are therapeutically effective in treatment of FSD or PMSA, wherein no more than one dosage form is administered on any day. Also provided is a kit useful in implementing such a treatment regimen. For example, a vaginal tablet was formulated containing 25 g estradiol, 1 mg methyltestosterone, and 2 mg tolterodine tartrate, useful as part of a treatment regimen for PMSA. The estradiol was delivered primarily locally for relief of vaginal dryness, soreness and/or irritation. The methyltestosterone was delivered systematically to increase libido. The tolterodine tartrate was delivered systematically to control urinary incontinence and thereby remove a source of anxiety contributing to PMSA. 124937-52-6, Tolterodine tartrate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vaginal compns. containing androgen, estrogen, and antimuscarinic for treatment of postmenopausal sexual dysfunction)

124937-52-6 CAPLUS

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L11
      2003:376565 CAPLUS
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      Antimuscarinic inhalants for treatment of urinary disorder
      Cammarata, Sue K.; Kolbasa, Karen; Palandra, Joe; Richards, Ivan; Warchol,
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      Mark P.
      Pharmacia & Upjohn Company, USA
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                                                                              20021104
                                                   US 2001-337298P
                                                                              20011105
                                                   wo 2002-us35335
                                                                              20021104
                                                   US 2002-287061
     US 2003144352
                              Α1
                                     20030731
                                                                               20021104
                                                   US 2001-337298P
                                                                              20011105
                                                   EP 2002-776444
     EP 1441706
                              A2
                                     20040804
                                                                              20021104
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
                                                   US 2001-337298P
                                                                           P 20011105
                                                   wo 2002-us35335
                                                                              20021104
     JP 2005511582
                              T2
                                     20050428
                                                   JP 2003-541756
                                                                              20021104
                                                   US 2001-337298P
                                                                           Ρ
                                                                              20011105
     WO 2002-US35335 W 20021104
The present invention concerns the use of antimuscarinic agents for the treatment of urinary disorders. The invention provides a method of treating urinary disorder in a mammal, including man, comprising administering to said mammal, in need of such a. treatment, a
AB
     therapeutically effective amount of an antimuscarinic agent, or solvate or
     prodrug thereof, said administration being performed by inhalation or
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insufflation. Furthermore, the present invention provides a pharmaceutical composition for treating urinary disorder in a mammal, including man, which is in the form of an inhalable or insufflable preparation and comprises a therapeutically effective amount of an antimuscarinic agent, or solvate or prodrug thereof, together with an inhalably or insufflably acceptable carrier or diluent therefor. The invention also provides a novel use of an antimuscarinic agent, or solvate or prodrug thereof, for the manufacture of an inhalable or insufflable medicament for therapeutical treatment of urinary disorders. Tolterodine L-tartrate for aerosol administration was prepared, and administered to patients with overactive bladder to examine the pharmacokinetics. 124937-52-6

IT

RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antimuscarinic inhalants for treatment of urinary disorder)

RN 124937-52-6 CAPLUS

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 C4 H6 O6 CMF

Absolute stereochemistry.

L11 ANSWER 61 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

2003:335062 CAPLUS AN

DN 138:353732

Quaternary ammonium compounds and their use as antimuscarinic agents Richards, Ivan; Cammarata, Sue K.; Wegner, Craig D.; Hawley, Michael; Warchol, Mark P.; Kontny, Mark; Morozowich, Walter; Kolbasa, Karen P.; Moon, Malcolm W.; Bonafoux, Dominique; Wolfson, Sergey G.; Lennon, Patrick ΤI TN

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Pharmacia & Upjohn Company, USA
PA
       PCT Int. Appl., 69 pp.
SO
       CODEN: PIXXD2
DT
       Patent
       English
LA
FAN.CNT 1
                                                                                          DATE
                                 KIND DATE
                                                          APPLICATION NO.
       PATENT NO.
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       wo 2003035599
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                                           20030501 WO 2002-US34529
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                 UG, US, UZ, VN, YU, ZA, ZM, ZW
            RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
                 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
                 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
                 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-348930P

US 2002-361979P

US 2002-391521P

223 AA 20030501 CA 2002-2464223
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BR 2002-6207
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            R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK US 2001-348930P P 2
                                                                                      P 20011026
                                                           US 2002-361979P
                                                                                      Ρ
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JP 2003-538115
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US 2002-391521P
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                                                                                      Ρ
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                                                                                      Ρ
                                                           wo 2002-US34529
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                                                           NO 2003-2938
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                                                                                      Ρ
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                                                           wo 2002-US34529
US 2005-74914
US 2001-348930P
US 2002-361979P
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                                                                                          20021025
      us 2005148672
                                  Α1
                                           20050707
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                                                                                          20020306
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                                                                                          20020625
                                                           us 2002-280906
                                                                                     A1 20021025
      MARPAT 138:353732
os
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Absolute stereochemistry. Rotation (+).

CMF C22 H31 N O

CRN 87-69-4 CMF C4 H6 06

Absolute stereochemistry.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 62 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:285824 CAPLUS
DN 139:30512
TI The use of tolterodine in children after oxybutynin failure
AU Bolduc, S.; Upadhyay, J.; Payton, J.; Bagli, D. J.; McLorie, G. A.;
Khoury, A. E.; Farhat, W.
CS Division of Urology, The Hospital for Sick Children, University of
Toronto, Toronto, ON, Can.
SO BJU International (2003), 91(4), 398-401

CODEN: BJINFO; ISSN: 1464-4096

PB Blackwell Publishing Ltd.

DT Journal LA English

This work assessed the safety and efficacy of tolterodine tartrate prescribed to children with dysfunctional urinary voiding who previously had failed to tolerate oxybutynin chloride. The 34 patients were treated with oxybutynin for a median (range) of 6 (2-84) mo. When significant side-effects were reported, they were crossed over to tolterodine. The mean age at the 1st dose of tolterodine was 8.9 yr; the dose was 1 mg twice daily for 12 patients and 2 mg twice daily for 22. The median treatment with tolterodine was 11.5 mo, with 20 (59%) patients reporting no side-effects; six described the same but tolerable side-effects as with oxybutynin. Eight patients discontinued tolterodine because of side-effects after a median (range) of 5 (1-11) months. The efficacy of tolterodine was comparable with that of oxybutynin diaries. The reduction in wetting episodes after 1 yr was >90% in 23 (68%) of the patients, more than half in five and less than half (or failure) in six patients. Tolterodine is tolerated well in children. In this subgroup of patients who could not tolerate oxybutynin, 77% were able to continue tolterodine treatment with no significant side-effects.

IT 124937-52-6. Tolterodine tartrate

124937-52-6, Tolterodine tartrate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (tolterodine efficacy and side effects in children with bladder dysfunction who were intolerant to oxybutynin)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 63 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2003:261600 CAPLUS
AN
      138:276286
DN
      Pharmaceutical compositions containing muscarinic antagonists and
TI
      5\alpha-reductase inhibitors for urinary tract disorder treatment
      Arneric, Stephen P.; Andersson, Per-Olof
IN
PA
      Pharmacia AB, Swed.
SO
      PCT Int. Appl., 23 pp.
      CODEN: PIXXD2
DT
      Patent
      English
LA
FAN.CNT 2
                               KIND
                                                      APPLICATION NO.
                                                                                   DATE
      PATENT NO.
                                       DATE
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                                       20030403
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      wo 2003026564
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      wo 2003026564
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      wo 2003026564
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                CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
                GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
                LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
               PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
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                                                      us 2001-965556
                                                                               A 20010927
                                                      SE 2001-3858
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                                       20030327
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                                                      WO 2002-SE1748
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               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
US 2001-965556 A 20010927
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PATENT FAMILY INFORMATION:
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FAN 2003:242003

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PATENT NO.
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       wo 2003026564
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                  PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
                  UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
            RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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                  FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
                 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG US 2001-965556
                                                                                            20010927
                                                            SE 2001-3858
EP 2002-775633
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                                   Α2
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                                                            us 2001-965556
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                                                            us 2001-965556
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       US 2004116533
                                   A1
                                           20040617
                                                            us 2003-729764
                                                                                            20031205
                                                            us 2001-965556
                                                                                       A1 20010927
       ZA 2004002362
                                           20050120
                                                            ZA 2004-2362
                                                                                            20040325
                                   Α
                                                            us 2001-965556
                                                                                       Α
                                                                                           20010927
      The present invention concerns the field of urol. The invention provides a pharmaceutical composition comprising a combination of a first compound selected from the group consisting of muscarinic receptor antagonists, 5\alpha-reductase inhibitors, and \alpha-adrenergic receptor antagonists, and precursors and salts, and a second compound selected from the group consisting of 5-HT1a receptor agonists and antagonists, and precursors and salts thereof and optionally a carrier or a diluent
AB
       precursors and salts thereof, and optionally a carrier or a diluent.
       There is also provided a method of treatment of urinary disorders in a
       mammal, including humans. A pharmaceutical composition is prepared by
combining
       tolterodine with a neutral 5-HT1a receptor antagonist in a carrier.
       composition contains 0.05-4 mg tolterodine/kg patient body weight (e.g., 3-240
mg
       tolterodine for a person weighing 60 kg) and 0.01-1 mg of neutral 5-HT1a
       receptor antagonist/kg of patient body weight The composition is administered
to
       a patient for the treatment of incontinence, and particularly stress
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incontinence, urge incontinence or mixed incontinence.

IT 124937-52-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical compns. containing muscarinic antagonists and 5α -reductase inhibitors for urinary tract disorder treatment)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 64 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2003:19961 CAPLUS

DN 138:78464

TI Pharmaceutical preparations based on active ingredients susceptible to illicit administration

IN Garavani, Alberto; Marchiorri, Maurizio; Di Martino, Alessandro

PA Altergon S.A., Switz.

SO Eur. Pat. Appl., 11 pp. CODEN: EPXXDW

DT Patent

LA English

FAN CNT 1

FAN.	CNT 1				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	EP 1273301	A2	20030108	EP 2002-15073	20020705
	EP 1273301	А3	20030409		
	EP 1273301	В1	20060906		
	R: AT, BE, CH,	DE, DK	, ES, FR, GB	, GR, IT, LI, LU, NL, S	SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
IT 2001-MI1446 A 20010706
AT 338567 E 20060915 AT 2002-15073 20020705
IT 2001-MI1446 A 20010706

Disclosed are pharmaceutical formulations for oral administration, preferably in the form of a soft capsule enclosing an active principle susceptible to illicit administration and at least one pharmaceutically acceptable organoleptic marker which is particularly evident for its odor, taste or color or for its scarce miscibility with food. The active principle is selected from the group consisting of a substance acting on the central nervous system and/or as a narcotic and of a substance with anabolizing activity or the like. The organoleptic marker is independently selected out of one or more substances belonging to the group consisting of flavoring agents, flavoring agents, coloring agents, oddrants, and oils

odorants, and oils.
IT 124937-52-6, Tolterodine tartrate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical prepns. based on active ingredients susceptible to illicit administration containing organoleptic markers)

RN 124937-52-6 CAPLUS

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CN

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 65 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN AN 2002:945736 CAPLUS DN 139:159672

- Therapeutic Efficacy Of Extended Release Oxybutynin Chloride, And TI Immediate Release And Long Acting Tolterodine Tartrate In Children With Diurnal Urinary Incontinence
- ΑU
- Reinberg, Y.; Crocker, J.; Wolpert, J.; Vandersteen, D. The Center for Pediatric Urology, Pediatric Surgical Associates, CS Minneapolis, MN, 55404, USA
- Journal of Urology (Hagerstown, MD, United States) (2002), Volume Date 2003, 169(1), 317-319
 CODEN: JOURAA; ISSN: 0022-5347
 Lippincott Williams & Wilkins SO
- PB
- DT Journal
- English LA We compare the tolerability and efficacy of extended release oxybutynin AB chloride, and immediate release and long acting tolterodine tartrate in children with non-neurogenic diurnal urinary incontinence and symptoms of overactive bladder. Children with a history of diurnal urinary incontinence were arbitrarily assigned to extended release oxybutynin, immediate release tolterodine or long acting tolterodine. The dose was titrated until effective (onset of complete diurnal urinary continence), maximal recommended dosage was achieved or bothersome anticholinergic side effects developed. An independent observer recorded the dose used, anticholingeric side effects and efficacy of therapy (incidence of urinary frequency, urgency, posturing and urinary incontinence). The study included 86 girls and 46 boys. There were no statistically significant differences among the 3 treatment groups regarding the presence of peripheral or central nervous system anticholinergic side effects. Extended release oxybutynin and long acting tolterodine were significantly more effective at reducing daytime urinary incontinence than immediate release tolterodine (p < 0.01 and p < 0.05, resp.). Extended release oxybutynin was significantly more effective then long acting tolterodine for complete resolution of diurnal incontinence (p < 0.05). Thus, extended
- immediate release tolterodine in decreasing diurnal urinary incontinence. Extended release oxybutynin chloride is more effective than either immediate or long acting tolterodine for control of daytime urinary incontinence and urinary frequency. 124937-52-6, Tolterodine tartrate IT RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (therapeutic efficacy of extended release oxybutynin chloride, and immediate release and long acting tolterodine tartrate in children with diurnal urinary incontinence)

release oxybutynin and long acting tolterodine are more effective than

- 124937-52-6 CAPLUS RN
- Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 66 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN
      2002:849709 CAPLUS
      137:353828
DN
      Poly(alkylene oxide) having reduced formic compound content for release
TI
      dosage form
      Fan, You-Ling
IN
      Union Carbide Chemicals & Plastics Technology Corporation, USA
PA
S0
      PCT Int. Appl., 25 pp.
      CODEN: PIXXD2
DT
      Patent
      English
LA
FAN.CNT 1
                                                                                        DATE
      PATENT NO.
                                 KIND
                                          DATE
                                                          APPLICATION NO.
                                          20021107
                                                         WO 2002-US13444
                                                                                         20020429
PΙ
      wo 2002088217
                                  Α1
                AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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US 2001-287885P P 20010501

EP 2002-734076

wo 2002-US13444

20020429

EP 1385898

EP 1385898

AB

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T2 20041007 JP 2002-585514 20020429 JP 2004530748 US 2001-287885P 20010501 WO 2002-US13444 W 20020429 AT 328028 F 20060615 AT 2002-734076 20020429 20010501 US 2001-287885P Title particle comprises (i) a polymer polymerized from an alkylene oxide monomer having weight average weight 100,000-1,000,000 g/g mol and (ii) 0-200 ppm (based on total weight of the particle) formic compound, such as formic acid and its salts and esters, wherein the particle has a core and an shell with concentration gradient of the formic compound (the core contains higher formic compound content than shell). The method for reducing formic compound on surface of the polyoxyalkylene particle comprises treating the particle with an acid having pKa lower than the pKa of formic acid. Thus, a slurry containing 70 parts PKA N 80NF (polyethylene oxide) with inorg. formate level >500 ppm was mixed with 20 mL hydrochloric acid (37%) and 480 mL iso-Pr alc. at room temperature for 60 min and washed to give a polymer with inorg. formate content <150 ppm. 124937-52-6, Tolterodine tartrate RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (poly(alkylene oxide) having reduced formic compound content obtained by treating with acid for release dosage form)
124937-52-6 CAPLUS

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,

(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9cí) (CÁ INDEX NAME)

CM

124937-51-5 CRN C22 H31 N O CMF

Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 C4 H6 O6 CMF

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 67 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
         2002:728118 CAPLUS
         137:257572
DN
         Treatment of overactive bladder with once-daily extended-release
TI
         tolterodine or oxybutynin: the antimuscarinic clinical effectiveness trial
         Sussman, David; Garely, Alan
ΑU
         Department of Surgery, Division of Urology, University of Medicine and Dentistry of New Jersey, Stratford, NJ, 08084, USA
Current Medical Research and Opinion (2002), 18(4), 177-184
SO
         CODEN: CMROCX; ISSN: 0300-7995
         LibraPharm Ltd.
PB
DT
         Journal
LA
         Enalish
         Treatment with the antimuscarinic agents tolterodine and oxybutynin is the
AB
         mainstay of therapy for overactive bladder, a chronic and debilitating condition characterized by urinary urgency with or without urge
         incontinence, usually in combination with urinary frequency and nocturia.
        This study consisted of two trials; in one, patients with overactive bladder were randomized to 8 wk of open-label treatment with either 2 mg or 4 mg of once-daily extended-release tolterodine (TER), and in the other to 5 mg or 10 mg of extended-release oxybutynin (OER). The study protocol and design were identical for the two trials and site selection ensured
         that there was no bias in either trial for the tendency of investigators
        to prescribe one drug rather than the other, or for geog. location. A total of 1289 patients were enrolled, 669 in the tolterodine trial (TER 2
        mg, n = 333; TER 4 mg, n = 336) and 620 in the oxybutynin trial (OER 5 mg,
        n=313; OER 10 mg, n=307). Fewer patients prematurely withdrew from the trial in the TER 4 mg group (12%) than either the OER 5 mg (19%; p=0.01) or OER 10 mg groups (21%; p=0.002). More patients in the OER 10 mg group than the TER 4 mg group withdrew because of poor tolerability (13% vs. 6%; p=0.001). After 8 wk, 70% of patients in the TER 4 mg
        group perceived an improved bladder condition, compared with 60% in the TER 2 mg group, 59% in the OER 5 mg group and 60% in the OER 10 mg group
         (all p < 0.01 vs TER 4 mg). Response to therapy was greater in a subgroup of patients whose perception of bladder condition was moderate to severe
        at baseline (TER 4 mg 77% vs OER 10 mg 65%; p < 0.01). Dry mouth was dose-dependent with both agents, although differences between doses only reached statistical significance in the oxybutynin trial (OER 5 mg vs OER
        10 mg; p = 0.05). Patients treated with TER 4 mg reported a significantly lower severity of dry mouth compared with OER 10 mg. In conclusion, the greater efficacy and tolerability of tolterodine ER 4 mg suggests improved clin. effectiveness compared with oxybutynin ER 10 mg.
        124937-52-6, Tolterodine tartrate
IT
        RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
         activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
              (tolterodine or oxybutynin once-daily extended-release in treatment of
              overactive bladder)
        124937-52-6 CAPLUS
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        Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
         (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
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Absolute stereochemistry. Rotation (+).

124937-51-5

C22 H31 N O

CRN

CMF

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 68 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
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      2002:609156 CAPLUS
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      138:254881
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      Synthetic study on M-receptor antagonist tolterodine tartrate
      Zhou, Xinbo; Gao, Wenfang; Zheng, Hong; Zhang, Yinghua
School of Pharmaceutical Engineering, Shenyang Pharmaceutical University,
ΑU
CS
      Shenyang, 110016, Peop. Rep. China
Zhongguo Yaowu Huaxue Zazhi (2002), 12(2), 107-109
S0
      CODEN: ZYHZEF; ISSN: 1005-0108
PB
      Zhongguo Yaowu Huaxue Zazhi Bianjibu
      Journal
DT
      Chinese
LA
os
      CASREACT 138:254881
      Tolterodine was synthesized through cyclization, methylation,
AB
      chlorination, amidation, reduction, demethylation, and separation from the
starting
      material cinnamic acid and p-cresol with an overall yield 14.4%.
      improved methods were presented for the preparation of the two key
      intermediates, 6-methyl-4-phenyl-3,4-dihydrocoumarin and N,N-diisopropyl-3-(2-methoxy-5-methylphenyl)-3-phenylpropionamine HCl (8).
      124937-52-6P, Detrol
IT
      RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
      study); PREP (Preparation); USES (Uses)
         (synthesis of tolterodine tartrate as M-receptor antagonist)
RN
      124937-52-6 CAPLUS
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
     CM
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Page 135

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 69 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN AN 2002:556104 CAPLUS DN 137:109489

Compositions comprising a polypeptide and an active agent TI

IN Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J.

PA

U.S. Pat. Appl. Publ., 34 pp. **S**0

CODEN: USXXCO

DT Patent

English LA

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Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

IT 124937-52-6, Tolterodine tartrate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. comprising a polypeptide and an active agent)

RN 124937-52-6 CAPLUS

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Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 70 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN AN 2002:332011 CAPLUS

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              SN, TD, TG
                                                 US 2003-507012P
                                                                           20030930
                                                    2004-567800P
                                                                           20040505
                                                                       Ρ
                                                 US
                                                    2004-567802P
                                                                       Ρ
                                                                          20040505
                                                 US
                                                 US 2004-568011P
                                                                          20040505
                                                                       Ρ
     us 2005176645
                            A1
                                   20050811
                                                 us 2004-953116
                                                                           20040930
                                                 US 2002-358368P
                                                                           20020222
                                                 US 2002-362082P
                                                                       Ρ
                                                                           20020307
                                                 WO 2003-US5525
                                                                       A2 20030224
                                                 US 2003-507012P
                                                                       Ρ
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                                                 US 2004-567800P
                                                                       Ρ
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                                                 US 2004-568011P
                                                                           20040505
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                                                 us 2004-927257
                                                                       Α2
                                                                          20040827
                                                    2004-953119
     us 2005176646
                            A1
                                   20050811
                                                 US
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                                                    2003-507012P
                                                                       Ρ
                                                 US
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                                                 US 2004-567800P
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                                                 US 2004-567802P
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     us 2005176644
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                                   20050811
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                                                 US 2003-507012P
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                                                 US 2004-567802P
                                                                       Ρ
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                                                 us 2004-953110
     us 2005266070
                            Α1
                                   20051201
                                                                           20040930
                                                    2003-507012P
2004-567800P
                                                 US
                                                                       Ρ
                                                                           20030930
                                                 US
                                                                       P
                                                                           20040505
                                                 US 2004-568011P
                                                                       Ρ
                                                                          20040505
     Claimed are compns. comprising a polypeptide and an active agent
AB
     covalently attached to the polypeptide and a method for delivery of an
     active agent to a patient by administering the composition to the patient.
                                                                                          The
     peptide is a homopolymer of a naturally occurring amino acid or a
     heteropolymer of two or more naturally occurring amino acids.
     example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin
     hydrochloride.
IT
     124937-52-6, Tolterodine tartrate
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
     (compns. comprising a polypeptide and an active agent) 124937-52-6 CAPLUS
RN
     Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
     (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
     CM
          124937-51-5
     CRN
     CMF
          C22 H31 N O
Absolute stereochemistry. Rotation (+).
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2 CM

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 71 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

2002:314176 CAPLUS AN

137:41178 DN

Once-daily, extended-release formulations of antimuscarinic agents in the treatment of overactive bladder: a review TI

ΑU Rovner, Eric S.; Wein, Alan J.

Division of Urology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104, USA European Urology (2002), 41(1), 6-14 CS

S0

CODEN: EUURAV; ISSN: 0302-2838

PΒ Elsevier Science B.V.

DT Journal; General Review

English LA

A review. Overactive bladder (OAB) is a chronic condition that often requires long-term treatment to maintain control of symptoms. A range of therapeutic options are available; however, antimuscarinic agents form the mainstay of treatment. Of these agents, tolterodine and oxybutynin are the most widely used. It is well documented that the immediate-release AB (IR) formulations of these agents have equivalent efficacy in relieving OAB symptoms. However, tolterodine demonstrates a more favorable tolerability profile, particularly in terms of the frequency and severity of dry mouth. Due to the development of novel drug delivery systems, extended-release (ER) formulations of both oxybutynin and tolterodine are now available, permitting once-daily dosing. The convenience of once-daily dosing of antimuscarinic agents would be expected to improve patient compliance and further relieve the symptoms of OAB. Clin. studies with the ER formulations of tolterodine and oxybutynin demonstrate potential clin. advantages over their resp. IR forms in terms of either efficacy or tolerability or both, although the therapeutic index of tolterodine ER appears to show a greater advantage over its IR counterpart compared with oxybutynin ER and its IR form. Importantly, the two ER agents have not

been compared directly in a head-to-head clin. study. Overall, available clin. data suggest that the newly developed ER formulation of tolterodine represents a significant therapeutic advancement in the treatment of OAB.

IT 124937-52-6, Tolterodine tartrate

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Detrol; once-daily, extended-release formulations of antimuscarinic agents in treatment of overactive bladder in women)

RN

124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME) CN

CM

124937-51-5 CRN CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 72 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

2001:844452 CAPLUS ΑN

136:299846 DN

Determination of levo-enantiomer in tolterodine tartrate by HPCE TI

Huang, Zongyu; Du, Jiaqiu; Cai, Wen ΑU

Zhejiang Institute for Drug Control, Hangzhou, 310004, Peop. Rep. China Yaowu Fenxi Zazhi (2001), 21(5), 351-354
CODEN: YFZADL; ISSN: 0254-1793 CS

PB Yaowu Fenxi Zazhi Bianji Weiyuanhui

DT Journal

LA Chinese

A high performance capillary electrophoresis (HPCE) method for determination of

the levo-enantiomer of tolterodine tartrate was established. Both complexation and resolution were affected by the cyclodextrin (CD) type, CD concentration and the pH of electrolyte. The influence of working voltage and capillary temperature on the enantiomer separation was also analyzed. Electrophoretic medium was 0.1 mol L-1 trihydroxymethylaminomethane buffer (adjust pH to 3.0 with H3PO4) containing 20 mmol L-1 hydroxypropyl- β -cyclodextrin. An uncoated capillary was 57 cm x 50 μ m (50 cm to the detector). Detection was carried out with a UV detector at 204 nm. The separation was performed at 15° with a pos. voltage of 20 kV. Samples were injected into the capillary by pressure for 3 s. The enantiomers of tolterodine tartrate was separated well. The linear concentration region was 0.001-1.5 mg mL-1. The RSD for migratory time and peak response were < 4.1% and 4.9% resp. The recovery for levo-enantiomer was 102.1% (n=6). The lowest detective concentration was 0.5 μ g mL-1 for each enantiomer. This method was suitable for check levo-enantiomer in tolterodine tartrate in laboratorv

IT 124937-52-6, Tolterodine tartrate

RL: ANT (Analyte); ANST (Analytical study)

(determination of tolterodine tartrate by high performance capillary electrophoresis)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

L11 ANSWER 73 OF 82 CAPLUS COPYRIGHT 2006 ACS ON STN AN 2001:835896 CAPLUS

DN

Evidence for the efficacy and safety of tolterodine in the treatment of TI overactive bladder

ΔΠ

Abrams, Paul Bristol Urological Institute, Southmead Hospital, Bristol, BS10 5NB, UK CS

Expert Opinion on Pharmacotherapy (2001), 2(10), 1685-1701S0

CODEN: EOPHF7; ISSN: 1465-6566

Ashley Publications Ltd. PB

Journal; General Review DT

English LA

Overactive bladder (OAB) is a chronic and prevalent condition, AB A review. the symptoms of which (urinary frequency and urgency, with or without urge incontinence) can exert a profound neg. effect on a person's daily life activities. Tolterodine (Detrol in North America and Detrusito) in the rest of the world, Pharmacia), a competitive muscarinic antagonist, is the first agent of this class to be specifically developed for the treatment of OAB. This agent displays in vivo functional selectivity for the bladder over other tissues that contain muscarinic receptors (e.g., salivary glands, eye), which translates into good efficacy and tolerability in patients with OAB (including the elderly). Con Comparative, randomized, double-blind studies show that tolterodine (administered as immediate-release [IR] tablets 2 mg b.i.d.) is as effective as oxybutynin (5 mg t.i.d.) in improving all of the troublesome symptoms of OAB but with a significantly lower incidence and severity of dry mouth. The advent of a new extended-release (ER) capsule formulation of tolterodine (4 mg) for convenient once-daily treatment builds upon these findings, with significantly improved efficacy for reducing urge incontinence episodes and a lower frequency of dry mouth relative to the existing IR tablet (2 Tolterodine can therefore be considered a valuable, well-tolerated treatment option for patients with OAB, providing improvements in symptoms that are both clin. meaningful to patients and sustained during long-term treatment.

124937-52-6, Tolterodine tartrate IT

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Detrol; efficacy and safety of tolterodine in treatment of overactive

bladder in humans)

124937-52-6 CAPLUS RN CN

Phenol, 2-[(1R)-3-[bis(1-methy]ethy])amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

124937-51-5 CRN CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 74 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:460854 CAPLUS

DN 136:194075

TI A comparison of the effects on saliva output of oxybutynin chloride and tolterodine tartrate

AU Chancellor, Michael B.; Appell, Rodney A.; Sathyan, Gayatri; Gupta, Suneel

CS Department of Urology, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

SO Clinical Therapeutics (2001), 23(5), 753-760 CODEN: CLTHDG; ISSN: 0149-2918

PB Excerpta Medica, Inc.

DT Journal

LA English

AB

Oxybutynin chloride and tolterodine tartrate are anticholinergic agents used to suppress involuntary bladder contractions in urinary incontinence. They act by inhibiting binding of acetylcholine to the muscarinic receptors in the detrusor muscle of the bladder. The same types of muscarinic receptors are found in the salivary glands; thus anticholinergic agents may decrease saliva production and cause dry mouth, a commonly cited reason for discontinuation of therapy. The primary objective of this study was to compare saliva output, which is an objective measure of dry mouth, in subjects taking immediate- or extended-release oxybutynin, tolterodine, or placebo. This was a single-site, single-dose, randomized, double-blind, 4-treatment, 4-period crossover study. Subjects were randomly assigned to 1 of 4 treatment sequences that included extended-release oxybutynin 10 mg, tolterodine 2 mg, immediate-release oxybutynin 5 mg, and placebo. Saliva output was measured objectively before dosing with each treatment and at 0.5, 1, 2, 3, 4, 6, 8, 10, and 12 h after dosing. Thirty-six healthy adult volunteers (22 women and 14 men) participated in the study. They ranged in age from 19 to 42 yr (mean, 27 yr). Thirty-one were white, 3 Asian, and 2 black. There were no significant differences in predose saliva They ranged output between the 4 study groups. With placebo, saliva output increased throughout the day. Saliva output was maintained at predose levels throughout the day with extended-release oxybutynin. Two hours after dosing with tolterodine and immediate-release oxybutynin, saliva output decreased nearly 0.5 g in specimens collected over 2 min. All 3 active treatments were associated with lower saliva output compared with placebo. Extended-release oxybutynin and tolterodine were similar with respect to area under the saliva concentration-time curve but were associated with significantly greater saliva output than. Was immediate-release oxybutynin (P < 0.01). There were no serious adverse events (AEs) in this

IT

study. AEs were similar between treatments, although the incidence of headache was higher in the active-treatment groups than with placebo. Objective assessment of saliva output in healthy adult volunteers indicated that extended-release oxybutynin and tolterodine had less impact on saliva output than did conventional immediate-release oxybutynin, suggesting that they may yield lower levels of dry mouth. 124937-52-6, Tolterodine tartrate

RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); BIOL (Biological study)

(a comparison of the effects on saliva output of oxybutynin chloride and tolterodine tartrate)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 75 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:295441 CAPLUS

DN 135:205235

Prospective randomized controlled trial of extended-release oxybutynin chloride and tolterodine tartrate in the treatment of overactive bladder: results of the OBJECT study

AU Appell, Rodney A.; Sand, Péter; Dmochowski, Roger; Anderson, Rodney; Zinner, Norman; Lama, Daniel; Roach, Martha; Miklos, John; Saltzstein, Daniel; Boone, Timothy; Staskin, David R.; Albrecht, Detlef; Anderson,

CS S0

PB DT

LA

AB

Rodney; Antoci, Joseph; Appell, Rodney A.; Berger, Yitzhak; Bishop, Jay R., Jr.; Brown, Rodney; Childs, Stacy; Das, Anurag A.; Dennis, Rodney; Dmochowski, Roger; Dula, Eugene; Nuys, Van; Garely, Alan D.; Gittelman, Marc; Gottesman, James E.; Graham, Chester F.; Hagood, Paul G.; Harris, Richard; Karram, Mickey; Lama, Daniel J.; McMurray, James G.; Miklos, John; Munoz, David R.; Nehra, Ajay; Peters, Kenneth M.; Ritter, Henry; Roach, Martha; Saltzstein, Daniel; Sand, Peter; Sieber, Paul; Snyder, Jeffery; Spellberg, David; Tuttle, John; Staskin, David R.; Wainstein, Mark A.; White, Charles; Zinner, Norm Cleveland Clinic Foundation, Cleveland, OH, USA Mayo Clinic Proceedings (2001), 76(4), 358-363 CODEN: MACPAJ; ISSN: 0025-6196 Dowden Health Media, Inc. Journal English Objective: To compare the efficacy and tolerability of extended-release oxybutynin chloride and tolterodine tartrate at 12 wk in participants with overactive bladder. Subjects and Methods: The OBJECT (Overactive Bladder: Judging Effective Control and Treatment) study was a prospective, randomized, double-blind, parallel-group study was a prospective, randomized, double-blind, parallel-group study conducted between Mar. and Oct. 2000 at 37 US study sites. Participants who had between 7 and 50 episodes of urge incontinence per wk and 10 or more voids in 24 h received extended-release oxybutynin, 10 mg/d, or tolterodine, 2 mg twice daily. The outcome measures were the number of episodes of urge incontinence, total incontinence, and micturition frequency at 12 wk adjusted for baseline. Results: A total of 315 women and 63 men were randomized and treated, and 332 participants (276 women, 56 men) completed the study. At the end of the study, extended-release oxybutynin was significantly more effective the study, extended-release oxybutynin was significantly more effective than tolterodine in each of the main outcome measures: weekly urge incontinence (P=.03), total incontinence (P=.02), and micturition frequency episodes (P=.02) adjusted for baseline. Both drugs improved symptoms of overactive bladder significantly from baseline to the end of the study as assessed by the 3 main outcome measures (P<.001). Dry mouth, the most common adverse event, was reported by 28.1% and 33.2% of participants taking extended-release oxybutynin and tolterodine, resp. Rates of central nervous system and other adverse events were low and similar in both groups. Conclusions: Extended-release oxybutynin was more effective than tolterodine as measured by end-of-study urge incontinence, total incontinence, and micturition frequency episodes. Both groups had similar rates of dry mouth and other adverse events. 124937-52-6, Tolterodine tartrate RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oxybutynin chloride and tolterodine tartrate prospective randomized controlled trial in treatment of overactive bladder in humans) 124937-52-6 CAPLUS Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

IT

RN

CN

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 76 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
      2000:335217 CAPLUS
AN
DN
      132:339373
      New controlled release bead, a method of producing the same and multiple unit formulation comprising it
TI
      Gren, Torkel; Ringberg, Anders; Wikberg, Martin; Wald, Randy J.
IN
      Pharmacia & Upjohn AB, Swed.
PA
      PCT Int. Appl., 26 pp.
50
      CODEN: PIXXD2
DT
      Patent
LΑ
      English
FAN.CNT 5
      PATENT NO.
                               KIND
                                        DATE
                                                      APPLICATION NO.
                                                                                   DATE
                                        20000518
                                                      WO 1999-SE2052
                                                                                    19991111
PI
      wo 2000027364
                                A1
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                IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
               MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
                SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
           RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
                DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
               CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, SE 1998-3871
                                                                                   19981111
                                                      WO 1999-SE1463
WO 1999-SE1463
                                                                                   19990826
      wo 2000012069
                                       20000309
                                A1
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               MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
               SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW
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ES, FI, FF	, LS, MW, SD, SL, , GB, GR, IE, IT, , GN, GW, ML, MR,		BF, BJ, CF, CG,
CA 2350061 CA 2350061	AA 20000518 C 20050517		A 19980827 A 19981111 19991111
CA 2550001		SE 1998-3871 WO 1999-SE1463 WO 1999-SE2052	A 19981111 A 19990826 W 19991111
AU 2000014366 AU 762410	A5 20000529 B2 20030626	SE 1998-3871	19991111 A 19981111
BR 9915142	A 20010807	SE 1998-3871 WO 1999-SE1463	A 19990826 W 19991111 19991111 A 19981111 A 19990826
EP 1128819 EP 1128819 R: AT. BE. CH	A1 20010905 B1 20030820		W 19991111 19991111
	, LV, FI, RO	SE 1998-3871 WO 1999-SE1463	A 19981111 W 19990826
EE 200100254	A 20021216	WO 1999-SE2052 EE 2001-254 SE 1998-3871 WO 1999-SE1463	W 19991111 19991111 A 19981111 A 19990826
JP 2003517446 JP 3616011	T2 20030527 B2 20050202	WO 1999-SE2052 JP 2000-580595	W 19991111 19991111
NZ 511430	A 20030530	SE 1998-3871 WO 1999-SE1463 WO 1999-SE2052 NZ 1999-511430	A 19981111 A 19990826 W 19991111 19991111
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AT 247458	E 20030915	SE 1998-3871 WO 1999-SE1463	19991111 A 19981111 W 19990826
US 6911217	B1 20050628	WO 1999-SE2052 US 2001-763281 SE 1998-3871 WO 1999-SE1463	W 19991111 19991111 A 19981111 A 19990826
SK 284758	в6 20051103	WO 1999-SE2052 SK 2001-625 SE 1998-3871	W 19991111 19991111 A 19981111
TW 222879	в1 20041101	WO 1999-SE1463 WO 1999-SE2052 TW 2000-89102338 SE 1998-3871	A 19990826 A 19991111 20000211 A 19981111
CA 2387973	AA 20010517	CA 2000-2387973 WO 1999-SE2052 SE 2000-782	20001024 A 19991111 A 20000309
CZ, DE, DK	, DM, EE, ES, FI,	WO 2000-SE2061 WO 2000-SE2061 BB, BG, BR, BY, CA, GB, GD, GE, GH, GM, KZ, LC, LK, LR, LS,	HR, HU, ID, IL,

	SK, RW: GH, DE,	SL, TJ, GM, KE, DK, ES,	TM, TFLS, MV FI, FF	R, TT, TZ, V, MZ, SD, R, GB, GR,	NZ, PL, PT, RO, RU, UA, UG, US, UZ, VN, SL, SZ, TZ, UG, ZW, IE, IT, LU, MC, NL, ML, MR, NE, SN, TD,	YU, ZA AT, BE PT, SE	A, ZW E, CH, CY, E, BF, BJ,
	200101319 784104	2	A5 B2	20010606 20060202			
BR	200001534			20020625	WO 1999-SE2052 SE 2000-782 WO 2000-SE2061 BR 2000-15346 WO 1999-SE2052 SE 2000-782	Ŵ	
	1227806 1227806 R: AT.		A1 B1	20020807 20050803	WO 2000-SE2061 EP 2000-975092 GB, GR, IT, LI, LU,		20001024
	IE,	SI, LT,	LV, F	, RO, MK,	CY, AL WO 1999-SE2052 SE 2000-782		19991111 20000309
HU	200203028		A2	20030228	WO 2000-SE2061 HU 2002-3028 WO 1999-SE2052	W	20001024 20001024 19991111
JP	200351391	8	т2	20030415	SE 2000-782 WO 2000-SE2061 JP 2001-536139 WO 1999-SE2052	W	20000309 20001024 20001024 19991111
NZ	518309		Α	20030530	SE 2000-782 WO 2000-SE2061 NZ 2000-518309	A W	20000309 20001024 20001024
EE	200200245		Α	20030616	WO 1999-SE2052 SE 2000-782 WO 2000-SE2061 EE 2002-245 WO 1999-SE2052	A W	19991111 20000309 20001024 20001024 19991111
ΑT	300941		E	20050815	SE 2000-782 WO 2000-SE2061 AT 2000-975092 WO 1999-SE2052	A W	20000309 20001024 20001024 19991111
PT	1227806		т	20051031	SE 2000-782 WO 2000-SE2061 PT 2000-975092 WO 1999-SE2052	A W	20000309 20001024 20001024 19991111
ES	2245320		т3	20060101	SE 2000-782 ES 2000-975092 WO 1999-SE2052	A A	20000309 20001024 19991111
US	6630162		B1	20031007	SE 2000-782 US 2000-708428 WO 1999-SE2052 SE 2000-782		20000309 20001109 19991111 20000309
ZA	200100357	5	Α	20020503	US 2000-202862P ZA 2001-3575		20000510 20010503
NO	2001002314	4	Α	20010709	SE 1998-3871 NO 2001-2314 SE 1998-3871 WO 1999-SE1463	A W	19981111 20010510 19981111 19990826 19991111
	2001000333 20010333	3	A1 B1	20030430 20041031	WO 1999-SE2052 HR 2001-333	W	20010510

	BG	1055	82			Α		2001		WO WO BG SE WO WO	1998 1999 1999 2001 1998 1999	-SE14 -SE2(-105! -387: -SE14	463 052 582 L 463 052		A W A W	19981 19990 19991 20010 19981 19990 19991	0826 1111 0608 1111 0826
	НК	1040	917			A1		2005	0527	SE WO	2002 1998 1999 1999	3-3871 -SE14	L 163		A A	20020 19981 19990 19991	1111 0826
	ZA	2002	0027	67		Α		2003	0409	ZA	2002	-2767	7			20020 19991)409
	NO	2002	0022	64		Α		2002	0513	NO WO SE	2002 1999 2000 2000	-2264 -SE20 -782	1)52		W A	20020 19991 20000 20001	0513 1111 0309
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      MARPAT 132:339373
      A controlled release bead comprises: (i) a core unit of a substantially
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      water-soluble or water-swellable inert material; (ii) a first layer on the
      core unit of a substantially water-insol. polymer; (iii) a second layer
      covering the first layer and containing an active ingredient; and (iv) a third
      layer of polymer on the second layer effective for controlled release of
the active ingredient, wherein the first layer is adapted to control water
      penetration into the core. A method of producing the controlled release bead is also disclosed. A bead was prepared comprising a core of
      starch-cong. sugar sphere, a 1st layer containing Surelease, and 2nd layer containing tolterodine L-tartrate and HPMC, and a 3rd layer containing
      Surelease/HPMC.
      124937-52-6, Tolterodine tartrate
IT
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Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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ANSWER 77 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
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     Transdermally administered tolterodine as anti-muscarinic agent for the
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     Pharmacia & Upjohn Ab, Swed.; Orup Jacobsen, Lene
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AB A device for transdermal administration of tolterodine, optionally encompassing salts, prodrugs and metabolites thereof, optionally together with pharmaceutically acceptable carrier(s) to a human being or an animal in order to achieve an effect against overactive bladder is described. Examples are given for tolterodine permeation across membranes, dissoln. from drug-in-adhesive acrylates, and formulation of transdermal systems. 124937-52-6 IT

RL: DEV (Device component use); PEP (Physical, engineering or chemical process); PRP (Properties); THÚ (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(transdermal tolterodine as antimuscarinic agent for treatment of overactive bladder)

RN

124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R, 3R) -2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM

124937-51-5 CRN C22 H31 N O CMF

Absolute stereochemistry. Rotation (+).

2 CM

87-69-4 CRN С4 Н6 О6 CMF

Absolute stereochemistry.

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 3 ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 78 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11

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Therapeutic formulation for administering tolterodine with controlled TI release

Nilvebrant, Lisbeth; Hallen, Bengt; Olsson, Birgitta; Strombom, Jan; Kreilgard, Bo; Orup, Jacobsen Lene; Hoeck, Ulla; Kristensen, Helle; Gren, IN Torkel; Ringberg, Anders; Wikberg, Martin

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                  CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
            IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
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ΡΙ		2000 W:	O120 AE, CZ, IN, MG, SL, GH,	AL, DE, IS, MK, TJ, GM, FI.	AM, DK, JP, MN, TM, KE, FR.	A1 AT, DM, KE, MW, TR, LS, GB.	AU, EE, KG, MX, TT, MW,	2000 AZ, ES, KP, NO, UA, SD,	0309 BA, FI, KR, NZ, UG, SL,	BB, GB, KZ, PL, US, SZ,	WO BG GD LC PT UZ UG	1999 i, BF i, GE i, LF i, RC i, VN	 9-s 3, 5, 0,	E14 BY, GH, LR, RU, YU, AT,	CA, GM, LS, SD, ZA, BE,	CH HR LT SE ZW CH	, CM , HI , LI , SC	1999 N, CR J, ID J, LV G, SI	0826 , CU, , IL, , MD, , SK,
PI	WO	2000 W: RW:	0120 AE, CZ, IN, MG, SL, GH, ES,	AL, DE, IS, MK, TJ, GM, FI.	AM, DK, JP, MN, TM, KE, FR.	A1, DM, KE, MW, TR, LS, GB, GN,	AU, EE, KG, MX, TT, GW, GW,	2000 AZ, ES, KP, NO, UA, SD, IE,	0309 BA, FI, KR, NZ, UG, SL, IT, MR,	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BG GD LC PT UZ UG MC SN SE	1999 i, BF i, GE i, LF i, RC i, VN i, ZV i, NI i, TI 1998	 9-s 3, 5, 0, 4, 0, 2,	E14 BY, GH, LR, RU, YU, AT, PT,	64 CA, GM, LS, SD, ZA, BE, SE,	CH HR LT SE ZW CH BF	, CM , HI , LI , SC	1999 N, CR J, ID J, LV G, SI Y, DE J, CF	0826 , CU, , IL, , MD, , SK, , DK, , CG,
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ΡΙ	CA AU	2000 W: RW: 2341	0120 AE, CZ, IN, MG, SL, GH, ES, CI,	AL, DE, IS, MK, TJ, GM, FI.	AM, DK, JP, MN, TM, KE, FR.	A1 AT, DM, KE, MW, TR, LS, GB, GN,	AU, EE, KG, MX, TT, MW, GR,	2000 AZ, ES, KP, NO, UA, SD, IE, ML,	0309 BA, FI, KR, NZ, UG, SL, IT, MR,	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BG GD LC PT UZ MC SN SE CA SE WO	1998 , GE , CK , NI , TI 1998 1998	 9-s 3, 0,, 4,, 2,-2 3-2 3-2	E14 BY, GH, LR, RU, AT, PT, TG 864 341 864 E14	64 CA, GM, LS, SD, ZA, BE, SE,	CH HR LT SE ZW CH BF	, CN, LU, SO, SO, SO, SO, SO, SO, SO, A	1999 N, CR J, ID J, LV G, SI Y, DE 1, CF 1998 1999	0826 , CU, , IL, , MD, , SK, , DK, , CG, 0827 0826 0827
PI	CA AU	2000 W: RW:	0120 AE, CZ, IN, MG, SL, GH, ES, CI,	AL, DE, IS, MK, TJ, GM, FI.	AM, DK, JP, MN, TM, KE, FR.	A1 AT, DM, KE, MW, TR, LS, GB, GN,	AU, EE, KG, MX, TT, MW, GR,	2000 AZ, ES, KP, NO, UA, SD, IE, ML,	0309 BA, FI, KR, NZ, UG, SL, IT, MR,	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BG GD LC PT UZ UG SN SE CA SE WO AU SE	1998 , GE , CI , RO , VI , TI 1998 1998 1998 1998	 9-S 3, 5, 6, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1	E14 BY, GH, LR, RU, AT, PT, TG 2864 2864 E14	 64 CA, GM, LS, SD, ZA, BE, SE, 063	CH HR SE ZW CH BF	, CN, LU, SO, SO, SO, SO, SO, SO, SO, SO, SO, SO	1999 N, CR J, ID J, LV G, SI Y, DE 1998 1999 1998 1999	0826 , CU, , IL, , MD, , SK, , CG, 0827 0826 0827 0826
ΡΙ	CA AU AU	2000 w: RW: 2341 9958 7583	0120 AE, CZ, IN, MG, SL, GH, ES, CI,	AL, DE, IS, MK, TJ, GM, FI.	AM, DK, JP, MN, TM, KE, FR.	A1 AT, DM, KE, MW, TR, LS, GB, GN,	AU, EE, KG, MX, TT, MW, GR,	2000 AZ, ES, KP, NO, UA, SD, IE, ML, 2000 2000	0309 BA, FI, KR, NZ, UG, SL, IT, MR, 0309	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BG GD LC PT UZ WC SN SE CA SE WO AU SE WO	1998 , GE , CI , RC , VI 1998 1998 1998 1998 1998	 9-5 3, 5, 6, 6, 7, 8, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1	E14 BY, GH, LR, RU, YU, AT, PT, TG 2864 2864 8891	 64 CA, GM, LS, SD, ZA, BE, SE, 063	CH HR SE ZW CH BF	, CN, LN, SO, SO, SO, SO, SO, SO, SO, SO, SO, SO	1999 N, CR J, ID J, LV G, SI Y, DE 1998 1999 1998 1999 1999	0826 , CU, , IL, , MD, , SK, , CG, 0827 0826 0827 0826
PI	CA AU AU	2000 W: RW: 2341	0120 AE, CZ, IN, MG, SL, GH, ES, CI, 063	AL, DE, IS, MK, TJ, GM, FI, CM,	AM, DK, JP, MN, TM, KE, FR, GA,	A1 AT, DM, KE, MW, TR, LS, GB, GN, AA A1 B2	AU, EE, KG, MX, TT, MW, GR,	2000 AZ, ES, KP, NO, UA, SD, ML, 2000 2003	0309 BA, FI, KR, NZ, UG, SL, IT, MR, 0309	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BG GD C PT UZ UG SN SE CA SE WO AU SE WO EP	1998 , GE , CA , CA , CA , CA 1998 1998 1998 1998 1998 1998	 9-5 	E14 BY, GH, LR, RU, YU, AT, PT, TG 8864 881 8864 8891	CA, GM, LS, SD, ZA, BE, SE, 063	CH HR SE ZW CH BF	, C1, HU, LU, SC, SC, SC, SC, SC, SC, SC, SC, SC, SC	1999 N, CR J, ID J, LV G, SI 7, CF 1998 1999 1999 1999 1999	0826 , CU, , IL, , MD, , SK, , CG, 0827 0826 0827 0826
ΡΙ	CA AU AU	2000 W: RW: 2341 9958 7583	0120 AE, CZ, IN, MG, SL, GH, ES, CI, 063	AL, DE, IS, MK, TJ, GM, FI, CM,	AM, DK, JP, MN, TM, KE, FR, GA,	A1 AT, DM, KE, MW, TR, LS, GB, GN, AA	AU, EE, KG, MX, TT, MW, GR,	2000 AZ, ES, KP, NO, UA, SD, ML, 2000 2003	0309 BA, FI, KR, NZ, UG, SL, IT, MR, 0309	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BG GD LC PT UZ WO SN SE CA SE WO AU SE WO EP GR	1998 , GE , CI , RO , VI 1998 1998 1998 1998 1998 1998	 9-s 	E14 BY, GH, LR, RU, YU, AT, PT, TG 864 884 8891 864 861 864 861	CA, GM, LS, SD, ZA, BE, SE, 063	CH HR SE ZW CH BF	, Ch , LR , SG , Ch , A A W	1999 N, CR J, ID J, LV G, SI 1998 1999 1999 1999 1999 1999	0826 , CU, , IL, , SK, , DK, , CG, 0827 0826 0827 0826 0826 0827
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PI	CA AU AU	2000 W: RW: 2341 9958 7583	0120 AE, CZ, IN, MG, SL, GH, ES, CI, 063	AL, DE, IS, MK, TJ, GM, FI, CM,	AM, DK, JP, MN, TM, KE, FR, GA,	A1 AT, DM, KE, MW, TR, LS, GB, GN, AA A1 B2	AU, EE, KG, MX, TT, MW, GR,	2000 AZ, ES, KP, NO, UA, SD, ML, 2000 2003	0309 BA, FI, KR, NZ, UG, SL, IT, MR, 0309	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BGD LC PT UG SN SE SEA SWO AU SE SWO JP	1998 , GE , CI , RC , VI 1998 1998 1998 1998 1998 1998 1998 1998 1998 1998 1998	 9-s 3-s 5-s 5-s 6-s 6-s 6-s 6-s 6-s 6-s 6-s 6	E14 BY, GH, RU, RU, AT, PT, TG 864 864 861 864 861 465 LI, 864 671	 64 CA, GM, LS, SD, ZA, SE, 063 64 9	CH HR SE ZW CH BF	, CI, HU, CI, SI, SI, SI, SI, SI, SI, SI, SI, SI, S	1999 N, CR J, ID J, LV G, SI Y, DE 1998 1999 1999 1999 1999 1999 1999 199	0826 , CU, , IL, , SK, , CG, 0827 0826 0827 0826 0826 0827 0826 0826 0826
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PI	CA AU AU EP	2000 W: RW: 2341 9958 7583 1105 R:	0120 AE, CZ, IN, MG, SL, GH, ES, CI, 063 919 99	AL, DE, IS, MK, TJ, GM, FI, CM,	AM, DK, JP, MN, TM, KE, FR, GA,	A1 AT, DM, KE, MW, TR, LS, GB, GN, AA A1 B2 LV,	AU, EE, KG, MX, TT, MW, GR,	2000 AZ, ES, KP, NO, UA, SD, ML, 2000 2003 2001 ES, RO	0309 BA, FI, KR, NZ, UG, SL, IT, MR, 0309 0321 0320 0613 FR,	BB, GB, KZ, PL, US, SZ, LU, NE,	WO BGDC PTZ UG SE SEA SEO PTZ WO SE SWO DE GREEN WAY SEO SEO PTE SWO DE GREEN WAY AND THE SEO	1998 , GE , CI , RC , VI 1998 1998 1998 1998 1998 1998 1998 1998 1998 1998 1998	 9-s 	E14 BY, GH, RU, PT, TG 864 884 884 881 864 864 861 864 864 864 864 864 864 864 864 864 864	 64 CA, SD, SD, SE, 063 64 9 64 22 LU, 64 89	CH HR SE ZW CH BF	, HLLSC CY BS A W A W A W A W	1999 N, CR J, ID J, LV G, SI 1998 1999 1999 1999 1999 1999 1999 199	0826 , CU, , IL, , SK, , CG, 0827 0826 0827 0826 0827 0826 0827 0826 0827 0826 0827
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FAN	2000:335217			05 2001-703034	AI 20010430
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		•		WO 1999-SE1463 WO 1999-SE2052	A 19990826 W 19991111
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۸Т	247458		Ε	20030915	WO 1999-SE2052 AT 1999-971702	W	19991111
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	DE,	DK, E	5, FI,	FR, GB, GR,	IE, IT, LU, MC, NL, ML, MR, NE, SN, TD,	PI, SI	E, BF, BJ,
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	1227006		A 1	20020007	WO 2000-SE2061	W	20001024 20001024
	1227806 1227806		A1 B1	20020807 20050803	EP 2000-975092		20001024
L					GB, GR, IT, LI, LU,	NL. SI	E. MC. PT.
				FI, RO, MK,		,	-, ··-, · · ,
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	ES 2245320	т3	20060101	SE 2000-782 ES 2000-975092 WO 1999-SE2052	A 20000309 20001024 A 19991111 A 20000309
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	NO 2001002314	Α	20010709	SE 1998-3871 NO 2001-2314	A 19981111 20010510
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	HR 2001000333 HR 20010333	A1 B1	20030430 20041031	WO 1999-SE2052 HR 2001-333	W 19991111 20010510
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	BG 105582	Α	20011231	WO 1999-SE2052 BG 2001-105582 SE 1998-3871	W 19991111 20010608 A 19981111
	нк 1040917	A1	20050527	WO 1999-SE1463 WO 1999-SE2052 HK 2002-102521 SE 1998-3871 WO 1999-SE1463	W 19990826 W 19991111 20020404 A 19981111 A 19990826
	ZA 2002002767	Α	20030409	WO 1999-SE1403 WO 1999-SE2052 ZA 2002-2767 WO 1999-SE2052	A 19991111 20020409
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CZ, DE, IN, IS, MD, MG, SK, SL, RW: GH, GM, DK, ES,	DK, DM, EE JP, KE, KG MK, MN, MW TJ, TM, TR KE, LS, MW FI, FR, GB	, AZ, BA, , ES, FI, , KP, KR, , MX, NO, , TT, TZ, , SD, SL, , GR, IE,	WO 1999-SE2052 BB, BG, BR, BY, CA, GB, GD, GE, GH, GM, KZ, LC, LK, LR, LS, NZ, PL, PT, RO, RU, UA, UG, US, UZ, VN, SZ, TZ, UG, ZW, AT, IT, LU, MC, NL, PT, MR, NE, SN, TD, TG	CH, CN, CR, CU, HR, HU, ID, IL, LT, LU, LV, MA, SD, SE, SG, SI, YU, ZA, ZW BE, CH, CY, DE,
	AA		SE 1998-3871 WO 1999-SE1463	A 19981111 W 19990826 20001024 A 19991111 A 20000309 W 20001024
AU 2001013192 AU 784104	A5 B2	20010606 20060202	AU 2001-13192	20001024
BR 2000015346	Α .	20020625	WO 1999-SE2052 SE 2000-782 WO 2000-SE2061 BR 2000-15346 WO 1999-SE2052 SE 2000-782 WO 2000-SE2061	A 20000309 W 20001024 20001024 A 19991111 A 20000309 W 20001024
R: AT, BE,	A1 B1 CH, DE, DK LT, LV, FI	, ES, FR,	GB, GR, IT, LI, LU,	20001024 NL, SE, MC, PT, W 19991111
ни 200203028	Α2	20030228	SE 2000-782 WO 2000-SE2061 HU 2002-3028 WO 1999-SE2052 SE 2000-782	A 20000309 W 20001024 20001024 W 19991111 A 20000309
JP 2003513918	Т2	20030415	WO 2000-SE2061 JP 2001-536139 WO 1999-SE2052 SE 2000-782	W 20001024 20001024 A 19991111 A 20000309
NZ 518309	Α	20030530	WO 2000-SE2061 NZ 2000-518309 WO 1999-SE2052 SE 2000-782	W 20001024 20001024 A 19991111 A 20000309
EE 200200245	Α	20030616	WO 2000-SE2061 EE 2002-245 WO 1999-SE2052 SE 2000-782	W 20001024 20001024 A 19991111 A 20000309
AT 300941	E	20050815	WO 2000-SE2061 AT 2000-975092 WO 1999-SE2052 SE 2000-782	W 20001024 20001024 A 19991111
NO 2002002264	Α	20020513	WO 2000-SE2061 NO 2002-2264 WO 1999-SE2052 SE 2000-782 WO 2000-SE2061	A 20000309 W 20001024 20020513 W 19991111 A 20000309 W 20001024
2003:784592 PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2000-202862P
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                                                                                 19991111
                                       20000518
                                                     WO 1999-SE2052
     WO 2000027364
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SE 1998-3871

A 19981111
                                                     wo 1999-se1463
                                                                                 19990826
                                                                             W
      A method and formulation for treating unstable or overactive urinary
AB
      bladder, wherein tolterodine or a tolterodine-related compound, or a
      pharmaceutically acceptable salt thereof, is administered to a patient in
      a pharmaceutically effective amount thereof through a controlled release
      formulation that administers tolterodine or said tolterodine-related
      compound, or salt thereof, at a controlled rate for at least 24 h. A
      controlled-release capsule containing nonpareil beads coated by an Et
      cellulose layer, a tolterodine/HPMC layer, and a sustained-release Et cellulose/HPMC layer was prepared
      124937-52-6
IT
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (controlled-release tolterodine formulations)
      124937-52-6 CAPLUS
RN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
      (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)
      CM
            1
           124937-51-5
      CRN
      CMF
           C22 H31 N O
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Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 06

Absolute stereochemistry.

RE.CNT 4

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ANSWER 79 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN
L11
       1999:692703 CAPLUS
ΑN
       132:87770
DΝ
       Ketoconazole inhibits the metabolism of tolterodine in subjects with
ΤI
       deficient CYP2D6 activity
       Brynne, N.; Forslund, C.; Hallen, B.; Gustafsson, L. L.; Bertilsson, L.
ΑU
       Department of Clinical Pharmacology, Pharmacia and Upjohn AB, Stockholm,
CS
       SE-112 87, Swed.
       British Journal of Clinical Pharmacology (1999), 48(4), 564-572 CODEN: BCPHBM; ISSN: 0306-5251
SO
       Blackwell Science Ltd.
PB
       Journal
DT
       English
LA
       The pharmacokinetics and safety of tolterodine and tolterodine metabolites
AB
       was studied after single-and multiple-dose administration in the absence
       and presence of ketoconazole, an inhibitor of cytochrome P 450 (CYP) 3A4,
       in healthy volunteers with deficient CYP2D6 activity, i.e. poor metabolizers of debrisoquine. Eight healthy volunteers received single oral doses (2 mg) of tolterodine L-tartrate. Following a wash-out period of about 3 mo, six of the subjects participated in a multiple-dose (1 mg twice daily) phase of the study. Ketoconazole 200 mg was given once daily for 4-4.5 days during both the single and multiple dose tolterodine
       administration phases. Blood samples were drawn and the pharmacokinetics
       of tolterodine and its metabolites were determined A decrease (P < 0.01) in
       apparent oral clearance of tolterodine, from 10-12 1 h-1 to 4.3-4.7 l h-1,
       was obtained during concomitant administration of ketoconazole, yielding at least a two-fold increase in the area under the serum concentration-time
curve
       after single as well as after multiple doses following single dose
       administration of tolterodine. The mean (±s.d.) terminal half-life increased by 50% from 9.7±2.7 h to 15±5.4 h in the presence of ketoconazole. CYP3A4 is the major enzyme involved in the elimination of tolterodine in individuals with deficient CYP2D6 activity (poor metabolizers), since oral clearance of tolterodine decreased by 60% during
       ketoconazole coadministration. This inhibition resulted in 2.1-fold
       increase in AUC.
IT
       124937-52-6, Detrusitol
       RL: ADV (Adverse effect, including toxicity); BPR (Biological process);
       BSU (Biological study, unclassified); BIOL (Biological study); PROC
       (Process)
            (ketoconazole inhibits the metabolism of tolterodine in human subjects with
           deficient CYP2D6 activity)
       124937-52-6 CAPLUS
Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
[CA INDEX NAME]
RN
CN
       CM
             124937-51-5
       CRN
       CMF
              C22 H31 N O
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THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

Absolute stereochemistry. Rotation (+).

CRN 87-69-4 CMF C4 H6 O6

Absolute sterèochemistry.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 80 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1999:692702 CAPLUS

DN 132:87769

TI Fluoxetine inhibits the metabolism of tolterodine-pharmacokinetic implications and proposed clinical relevance

AU Brynne, N.; Svanstrom, C.; Aberg-Wistedt, A.; Hallen, B.; Bertilsson, L. Departments of Clinical Pharmacology, Pharmacia and Upjohn AB, Stockholm, SE-112 87, Swed.

SO British Journal of Clinical Pharmacology (1999), 48(4), 553-563 CODEN: BCPHBM; ISSN: 0306-5251

PB Blackwell Science Ltd.

DT Journal

LA English

The change in disposition of tolterodine during coadministration of the potent cytochrome P 450 2D6 (CYP2D6) inhibitor fluoxetine was studied. Thirteen patients received tolterodine L-tartrate 2 mg twice daily for 2.5 days, followed by fluoxetine 20 mg once daily for 3 wk and then concomitant administration for an addnl. 2.5 days. They were characterized as extensive metabolizers (EM1 with one functional CYP2D6 gene, EM2 with two functional genes) or poor metabolizers (PM). Nine patients, three EM2 and four EM1 and two PM, completed the trial. Following tolterodine administration, the area under the serum

concentration-time

curve (AUC) of tolterodine was 4.4-times and 30-times higher among EM1 and PM, resp., compared with EM2. The AUC of the 5-hydroxymethyl metabolite (5-HM) was not quantifiable in PM. Fluoxetine significantly decreased (P < 0.002) the oral clearance of tolterodine by 93% in EM2 and by 80% in EM1. The AUC of 5-HM increased in EM2 and decreased in EM1. However, the exposure to the active moiety (unbound tolterodine +5-HM) was not significantly increased in the two phenotypes. The subdivision of the EM group showed a 2.1-fold increase in active moiety in EM2 but the exposure

was still similar to EM1 compared with before the interaction. The study suggests a difference in the pharmacokinetics of tolterodine and its 5-hydroxymethyl metabolite depending on the number of functional CYP2D6 genes. Fluoxetine significantly inhibited the hydroxylation of tolterodine. Despite the effect on the pharmacokinetics of tolterodine in extensive metabolizers, the clin. effect is expected to be within normal variation.

IT 124937-52-6

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(fluoxetine inhibits the metabolism of tolterodine-pharmacokinetics)

RN 124937-52-6 CAPLUS

CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 81 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1997:743587 CAPLUS

DN 128:70329

TI Determination of tolterodine and the 5-hydroxymethyl metabolite in plasma, serum and urine using gas chromatography-mass spectrometry

AU Palmer, L.; Andersson, L.; Andersson, T.; Stenberg, U.

CS Department of Bioanalytical Chemistry, Pharmacia and Upjohn AB, Uppsala, S-751 82, Swed.

Journal of Pharmaceutical and Biomedical Analysis (1997), 16(1), 155-165 S0 CODEN: JPBADA; ISSN: 0731-7085

PB Elsevier Science B.V.

DT Journal

Enalish LA

A specific and sensitive capillary gas chromatog.-mass spectrometry assay AB for the determination of tolterodine and the 5-hydroxymethyl metabolite (Labcode

DD 01) in plasma, serum and urine is described. Extraction of the analytes was performed with liquid/liquid or solid-phase extraction prior to derivatization

with

a silyl reagent. The derivs. were quantified by selected ion monitoring mass spectrometry using deuterium-labeled internal stds. A single level calibration curve was utilised for quantification of plasma, serum and urine concns. of tolterodine and DD 01. The accuracy (inter- and intra-day) for both analytes was within 87-110% in the range 0.5 and 50 ng mL-1 and precision was better than 90%. Overall, this method was shown to be reliable for pharmacokinetic assays of tolterodine and the metabolite DD 01 in samples from preclin. and clin. studies.

124937-52-6, PNU 200583E IT

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(determination of tolterodine and the 5-hydroxymethyl metabolite in plasma,

serum and urine using gas chromatog.-mass spectrometry)

124937-52-6 CAPLUS RN

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R, 3R) - 2, 3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM

124937-51-5 CRN CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

87-69-4 CRN C4 H6 O6 CMF

Absolute stereochemistry.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 82 OF 82 CAPLUS COPYRIGHT 2006 ACS on STN L11 1990:55211 CAPLUS AN DN 112:55211 3,3-Diphenylpropylamines as drugs, especially anticholinergic agents, and their preparation and formulations containing them
Joensson, Nils Ake; Sparf, Bengt Ake; Mikiver, Lembit; Moses, Pinchas;
Nilvebrant, Lisbet; Glas, Gunilla TI IN KabiVitrum´AB, Swed. Eur. Pat. Appl., 37 pp. PA SO CODEN: EPXXDW DT Patent English LA FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ____ -----EP 325571 19890726 EP 1989-850017 19890120 PΙ Α1 EP 325571 В1 19910807 R: ES, GR SE 1988-207 A 19880122 3906644 W: AU, DK, FI, HU, JP, NO, US RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE SE 1988-207 19890727 WO 1989-SE16 wo 8906644 Α1 19890120 19880122 AU 8929329 **A1** 19890811 AU 1989-29329 19890120 AU 635493 19930325 В2 SE 1988-207 A 19880122 WO 1989-SE16 A 19890120 EP 354234 19900214 EP 1989-901611 19890120 Α1 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE SE 1988-207 JP 1989-501413 A 19880122 JP 03503163 T2 19910718 19890120 SE 1988-207 19880122 WO 1989-SE16 19890120 W AT 65990 19910815 AT 1989-850017 19890120 Ε SE 1988-207 19880122 EP 1989-850017 19890120 HU 58040 HU 1989-1069 **A2** 19920128 19890120 HU 212729 В 19961028 A 19880122 SE 1988-207 ES 2029384 Т3 19920801 ES 1989-850017 19890120 SE 1988-207 19880122 CA 1340223 Α1 19981215 CA 1989-588821 19890120 SE 1988-207 19880122 NO 9003085 19900711 NO 1990-3085 Α 19900711 NO 173496 19930913 В NO 173496 C 19931222 SE 1988-207 A 19880122 WO 1989-SE16 19890120 DK 9001725 19900719 DK 1990-1725 19900719 DK 172103 в1 19971027 SE 1988-207 19880122 wo 1989-SE16 19890120 FI 109900 В1 20021031 FI 1990-3688 19900720 SE 1988-207 19880122 WO 1989-SE16 19890120 W US 1991-810185 US 5382600 Α 19950117 19911219 SE 1988-207 19880122 us 1990-543767 B1 19900924

OS MARPAT 112:55211

AB The title compds. I (R1 = H, Me; R2-R4 = H, Me, MeO, OH, halo, carbamoyl, etc.; X = NR5R6; R5, R6 = non-aromatic hydrocarbyl, together containing ≥3 C atoms; or NR5R6 may form a ring) and physiol. acceptable acid addition salts, useful as drugs (especially as anticholinergics), were prepared A

3,3-bis-(2-methoxyphenyl)propyl p-toluenesulfonate and diisopropylamine in MeCN was heated at 80° for 4-6 days to give, after workup and treatment with oxalic acid, the title compound N,N-diisopropyl-3,3-bis-(2-methoxyphenyl)propylamine oxalate. I (R1 = H, R2 = R3 = H, R4 = OH, X = NMeCMe3) (II) exhibited an IC50 of 4.9 + 10-9 M in a test for anticholinergic activity in isolated guinea pig bladder. This compared to 5.2 + 10-7 M for terodiline; II also showed comparable Ca-antagonistic effect and lower toxicity. Formulations containing I are given.

IT 124937-52-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of, as drug, especially anticholinergic) 124937-52-6 CAPLUS

RN 124937-52-6 CAPLUS
CN Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
(2R,3R)-2,3-dihydroxybutanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

=> d l12 1-6 fbib ab hitstr

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ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
L12
       2006:600616 CAPLUS
AN
DN
       145:83107
       Preparation of tolterodine from protected benzylmethylphenol and
TI
       (diisopropylamino)ethyl halides or sulfonates
      Yamada, Tsukasa; Itaya, Nobushige; Tanaka, Masahide
IN
      Sumitomo Chemical Co., Ltd., Japan
PA
       Jpn. Kokai Tokkyo Koho, 10 pp.
S0
      CODEN: JKXXAF
DT
       Patent
       Japanese
LA
FAN.CNT 1
                                                            APPLICATION NO.
                                                                                            DATE
       PATENT NO.
                                  KIND
                                            DATE
PΙ
      JP 2006160622
                                   Α2
                                            20060622
                                                            JP 2004-350942
                                                                                            20041203
                                                            JP 2004-350942
                                                                                            20041203
os
      MARPAT 145:83107
      Tolterodine, useful for treatment of incontinence, is prepared by (1) treatment of benzylphenols I (R = OH-protecting group; A = H) with bases, (2) reaction with (Me2CH)2NCH2CH2X (X = halo, alkylsulfonyloxy, arylsulfonyloxy) (II), and (3) deprotection of the resulting I [R = same as above; A = CH2CH2N(CHMe2)2]. Thus, a mixture of 2-benzyl-4-methylanisole (III) and 3-benzyl-4-methylanisole (2.7:1), prepared by reacting 4-methylanisole and PhCH2OH, was dissolved in THF and treated with BuLi at 0° for 6 h. II (X = Cl) was added dropwise to the above reaction mixture at -78° and the reaction mixture was stirred at room temperature for
AB
      mixture at -78° and the reaction mixture was stirred at room temperature for
      1 h to give 98.5% (based on III) N,N-diisopropyl-3-(2-methoxy-5-
      methylphenyl)-3-phenylpropanamine as mixture with N,N-diisopropyl-3-(5-
      methoxy-2-methylphenyl)-3-phenylpropanamine (10:1). This mixture was
      dissolved in AcOH and treated with HBr under reflux for 3 h to give 85.7%
       racemic tolterodine. The racemate was further converted into
      optically-active tolterodine tartrate upon reaction with L-tartaric acid.
IT
      209747-05-7P
      RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN
       (Synthetic preparation); PREP (Preparation)
           (preparation of tolterodine from protected benzylmethylphenol and
           (diisopropylamino)ethyl halides or sulfonates using bases)
      209747-05-7 CAPLUS
RN
      Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
CN
       (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)
      CM
             1
      CRN
            124937-51-5
           C22 H31 N O
      CMF
Absolute stereochemistry. Rotation (+).
   OН
           Ρh
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Page 233
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CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

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ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
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2005:1209252 CAPLUS AN

144:16947 DΝ

Juvenile pig detrusor: Effects of propiverine and three of its metabolites Wuest, Melinda; Braeter, Manfred; Schoeberl, Christian; Ravens, Ursula Institute of Pharmacology and Toxicology, Dresden University of TI

ΑU CS

Technology, Dresden, Germany European Journal of Pharmacology (2005), 524(1-3), 145-148 S0

CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier B.V.

Journal DT

English LA

In isolated detrusor strips, propiverine is known to be effective to AB decrease contractions elicited by elec. field stimulation (EFS). Here we investigated whether the metabolites M-5, M-6 and M-14 of propiverine retain the pharmacol. properties of the parent compound also in juvenile organisms. EFS-induced contractions of detrusor strips from juvenile pigs are more sensitive to atropine than strips from mature pigs. The atropine-resistant component of contraction is also significantly larger in juvenile pigs. Propiverine, its metabolites M-5, M-14 and also tolterodine completely reduced detrusor contraction in juvenile pigs. M-6 almost did not affect atropine-resistant contractions. We conclude that juvenile pig detrusors possess a higher atropine-resistant component of EFS-elicited contraction. Nevertheless order of potency and efficacy of propiverine and its metabolites M-5 and M-14 are similar in juvenile and mature pigs, while M-6 only reduces atropine-sensitive contractions in the juvenile organism.

IT 209747-05-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (effects of propiverine and three of its metabolites on juvenile pig detrusor)

209747-05-7 CAPLUS

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

CM 1

124937-51-5 CRN CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

RN

CN

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN 2003:722238 CAPLUS AN DN 140:321103 Synthesis of tolterodine L-tartrate TI Yuan, Zhedong; Yu, Xiong; Wang, Qiang; Zhang, Xiuping IN

Shanghai Institute of Pharmaceutical Industry, Peop. Rep. China PA

Faming Zhuanli Shenqing Gongkai Shuomingshu, 8 pp. 50 CODEN: CNXXEV

Patent

DT

LA Chinese

FAN.CNT 1

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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	CN 1379018	Α	20021113	CN 2002-111560	20020429
				CN 2002-111560	20020429

os CASREACT 140:321103

The process comprises cyclizing trans-cinnamic acid with 4-methylphenol in the presence of H2SO4 at 120-150° to obtain 6-methyl-4-phenyl-3,4-dihydrocoumarin, methylating with di-Me sulfate in alc. or acetone to obtain 3-(2-methoxy-5-methylphenyl)-3-phenylphe AB with SOC12 and aminating with diisopropylamine to obtain N,N-diisopropyl-3-(2-methoxy-5-methylphenyl)-3-phenylpropanamide, reducing with KBH4 and Lewis acid (such as ZnCl2 or AlCl3) in solvent (such as THF, dioxane, or toluene) at 80-100° to obtain N,N-diisopropyl-3-(2methoxy-5-methylphenyl)-3-phenylpropanamine; demethylating with >40% HBr to obtain N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropanamine; and salifying with L-tartaric acid in alc. or 90-95% alc. 209747-05-7P IT

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(synthesis of tolterodine L-tartrate)

RN

209747-05-7 CAPLUS Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)CN

CM

124937-51-5 CRN CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

87-69-4 CRN CMF C4 H6 O6

Absolute stereochemistry.

ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN L12

2003:242003 CAPLUS AN

138:260465 DN

Pharmaceutical composition comprising receptor agonists and antagonists TI treatment of urinary disorder Arneric, Stephen P.; Andersson, Per-Olof

IN

PA

SO U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DT Patent

English LA

FAN	.CNT 2 PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
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	wo 2003026564 wo 2003026564 wo 2003026564	A2 A3 C2	20030403 20031211 20040617	wo 2002-SE1748		20020926

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                    PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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US 2001-965556 A 20010927
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US 2001-965556

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US 2001-965556

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JP 2005503424	Т2	20050203	WO 2002-SE1748 JP 2003-530203	W	20020926 20020926
. 2003303.2			US 2001-965556 SE 2001-3858	A A	20010927 20011120
			WO 2002-SE1748	W.	20020926
The present invent	ion cond	cerns the fi	eld of urol. The ir	ivent	ion provide

AB a novel pharmaceutical composition, comprising a pharmaceutically effective combination of (i) a first compound selected from the group consisting of muscarinic receptor antagonists, 5a-reductase inhibitors, and α -adrenergic receptor antagonists, and precursors and pharmaceutically acceptable salts thereof, and (ii) a second compound selected from the group consisting of 5-HTla receptor agonists and antagonists, and precursors and pharmaceutically acceptable salts thereof, and optionally a pharmaceutically acceptable carrier or diluent therefor. There is also provided a method of therapeutical treatment of urinary disorder in a mammal, including man, comprising administering to said mammal, including man, in need of such treatment, a therapeutically effective amount of a composition according to the invention. A pharmaceutical composition contained between about 2 mg to about 20 mg of 5a-reductase inhibitor and between about 0.5 mg to about 50 mg of neutral 5-HT1a receptor antagonist. The composition is administered to a patient for the treatment of urinary disorder.

IT 209747-05-7

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical composition comprising receptor agonists and antagonists treatment of urinary disorder)

209747-05-7 CAPLUS

Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-, CN (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)

CM

RN

CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

2 CM

CRN 87-69-4 C4 H6 O6 CMF

Absolute stereochemistry.

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L12
     ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS ON STN
      2001:359788 CAPLUS
AN
      134:371775
DN
     Pharmaceutical formulation containing tolterodine for bladder disorders
TI
     Nilvebrant, Lisbeth; Hallen, Bengt; Ölsson, Birgitta; Stroembom, Jan;
TN
     Gren, Torkel; Ringberg, Anders; Wikberg, Martin
PA
     Pharmacia AB, Swed.
     PCT Int. Appl., 23 pp.
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WO 1999-SE2052 A 19991111
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       The invention relates to a pharmaceutical formulation containing tolterodine
AB
       or a tolterodine-related compound, or a pharmacol. acceptable salt thereof,
       as active ingredient, in which the formulation exhibits a controlled in vitro release of the active ingredient in phosphate buffer at pH 6.8 of not less than about 80 after 18 h, and after oral administration to a patient is capable of maintaining a substantially constant serum level of the active moiety or moieties for 24 h. The invention also relates to the
       use of the pharmaceutical formulation for treating overactive bladder and
       gastrointestinal disorders. Controlled release beads and capsules
       comprising multilayers were prepared containing tolterodine L-tartrate were
       prepared
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       RL: BPR (Biological process); BSU (Biological study, unclassified); PEP
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Absolute stereochemistry. Rotation (+).

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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 Novel intermediate 3,4-dihydro-6-methyl-4-phenyl-2H-benzopyran-2-ol (I)
and an improved process for the preparation of tolterodine using I are claimed. Thus, a mixture of I and (Me2CH)2NH in MeOH was hydrogenated over Pd/C at 45-50° and 48° for ca. 10 h followed by addition of HCl to give
 tolterodine hydrochloride.
 209747-05-7P, (R)-Tolterodine L-tartrate
 RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of tolterodine via 3,4-dihydro-6-methyl-4-phenyl-2H-benzopyran-
    2-ol as an intermediate)
 209747-05-7 CAPLUS
 Phenol, 2-[(1R)-3-[bis(1-methylethyl)amino]-1-phenylpropyl]-4-methyl-,
 (2R,3R)-2,3-dihydroxybutanedioate (salt) (9CI) (CA INDEX NAME)
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CRN 124937-51-5 CMF C22 H31 N O

Absolute stereochemistry. Rotation (+).

CM 2

CRN 87-69-4 CMF C4 H6 O6

Absolute stereochemistry.

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